RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

Vol. 73 AUGUST 1959 No. 2

Cell Renewal and Acute Radiation Damage[1]

HENRY QUASTLER, M.D.

RADIOSENSITIVITY AND CELL PROLIFERATION

There is no biological structure or function which cannot be disturbed by ionizing radiation, but the doses needed to produce observable effects range over many orders of magnitude, from millirads to millions of rads. To kill a *Drosophila* egg in its most sensitive stage requires only about 100 rads; the fully mature form of the same insect can survive doses up to 100,000 rads. A cell in the intestinal crypts is fatally damaged by a dose of 1,000 rads; the same cell, after its transition into a villus cell (which takes but a few hours) can be exposed to 30,000 rads, and probably more, without suffering fatal effects. Such vast differences in sensitivity are of great interest in themselves, and they are of particular importance to the radiotherapist in attempts to utilize differences in sensitivity between cancer cells and surrounding normal tissue.

Several attempts have been made to rationalize differences in radiosensitivity. One of the earliest is still among the most successful, the law proposed by Bergonié and Tribondeau in 1906 (1). This law states that the radiosensitivity of cells is the greater (*a*) the greater their mitotic activity, (*b*) the greater the number of divisions they still will undergo, and (*c*) the less differentiated they are in form and function. Thus two parts of the law relate directly and the third implicitly to proliferation. Proliferative activity has remained one of the major criteria of radiosensitivity, but so many exceptions have been found that the relation between proliferation and radiosensitivity must be reduced to a weaker form: (*a*) *Many—but not all—radiosensitive cell systems are proliferating.* (*b*) *Many—but not all—proliferating cell systems are radiosensitive.*

TABLE I: RELATION BETWEEN RADIATION RESPONSE AND CELL PROLIFERATION IN SYSTEMS KNOWN TO BE RADIOSENSITIVE

Relation Established	Relation Excluded	Relation Doubtful
Leukopenia	Death of mature lymphocytes	Erythema, epithelitis
Thrombopenia	Early erythema	Fibrosis
Erythropenia	Death of differentiating embryonic cells	Pneumonitis
Sterilization	Effects on nervous and sensory tissue	Effects on reticulo - endothelial system
Epilation	Suppression of secretion	Late effects on blood vessels
Depletion of gastrointestinal epithelium	Shock	Cancer induction
Some effects on tumors	Bone and cartilage necrosis	Several lethal effects in animals:
Severe skin changes	Kidney damage	Oral death
Disturbed bone growth	Effects on infection and inflammation	Pulmonary death
Dental effects (rodents)	Liver changes	Esophageal death
Some effects on embryonic development		"5 to 8 day" death
		"Slow component"

[1] From the Biology Department, Brookhaven National Laboratory, Upton, N. Y. Research carried out under the auspices of the U. S. Atomic Energy Commission. Presented as part of a Symposium on Radiation Biology at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

Fig. 1. Autoradiograph of the small intestine of a mouse labeled with tritiated thymidine fourteen hours before sacrifice. Individual labeled cells are clearly recognizable; most are in the crypts, but some have migrated onto the villi. (Hematoxylin; A.R. 10 Kodak film; × *c.* 275)

The first statement is substantiated in Table I, in which are listed several systems of known radiosensitivity. In some cases a link between radiosensitivity and proliferation is definitely established; in others it is definitely excluded; in still others it is doubtful.

The second part of the proposition is substantiated in Table II, in which are listed several proliferative cell systems, of which some are highly radiosensitive and others are not, while in some the degree of radiosensitivity has not been established.

As more data are collected, both tables may have to be revised, but this will not affect the validity of the conclusion that no simple and general relation exists between cellular proliferation and radiosensitivity.

RADIATION EFFECTS AND MITOSIS

Mitosis is a conspicuous phase of proliferation, and irradiation is known to affect mitosis; indeed, some of these effects are among the radiation responses most studied. They are not simple; neither is the process of mitosis itself.

TABLE II: RADIOSENSITIVITY OF PROLIFERATIVE SYSTEMS

Sensitive	Relatively Resistant	Sensitivity Questionable
Erythropoietic Myelopoietic Thrombopoietic Lymphopoietic Gastrointestinal epithelium Some tumors	Same systems after pre-irradiation	Respiratory epithelium Uterine glands Adrenal cortex
Hair follicle Spermatogonia Oogonia	Some tumors Skin Embryonic anlage (as a system)	

The following list, largely after Swann (10), enumerates some conditions which must be fulfilled before mitosis can occur. The list is almost certainly incomplete.

General Conditions for Mitosis

1. Minimum overall growth
2. Energy reservoir built up
3. SH cycle in appropriate stage
4. Chromosome material duplicated (including protein and DNA)
5. Nuclear RNA built up
6. Centriole duplicated

There are at least 9 distinct radiation effects upon mitosis, either direct or becoming manifest during or after mitosis; and this list is probably incomplete also.

Radiation Effects Associated With Cell Division

1. Chromosome stickiness
2. Delay of mitosis
3. Breaks, bridges, fragments (breakage-fusion-breakage cycle)
4. Pluripolar mitoses
5. Genic imbalance following mitosis
6. Cell abortion during or after mitosis (related to 3, 4, 5 . . . ?)
7. Chromosome division without nuclear division
8. Nuclear division without cell division
9. Cell division followed by fusion

RADIATION EFFECTS AND S PHASE

Mitosis is not the only recognized critical phase of the cell proliferation cycle. In recent years it has been possible to identify another phase with equal precision; this is the so-called *S* phase, during which the cell synthesizes new chromosomal material. In most types of cell, well defined intervals separate the end of the *S* phase from the commencement of mitosis, and the end of mitosis

TABLE III: DISORGANIZATION OF PHASE SEQUENCE

Preceding Phase	Subsequent Phase						
	G_1	S	G_2	m	T	M	D (decay)
Presynthesis (G_1)	?	O	...	...	X	?	X
Synthesis (S)	X	?	O	...	X	X	X
Premitosis (G_2)	X	...	?	O	?	?	...
Mitosis (m)	O	...	...	...	O	...	X
Transition (T)	...	...	...	...	...	O	?
Mature (M)	...	...	...	...	...	...	O

O = Normal transitions.
X = Transitions definitely observed in irradiated cells.
? = Transitions suspected to occur in irradiated cells.
... No transitions observed

from the commencement of the S phase. The most successful method of identifying cells in S phase is based on labeling with tritiated thymidine followed by high resolution autoradiography (3). Thymidine is known to be incorporated almost exclusively into large molecules of a single species, deoxyribosenucleic acid (DNA), which is a characteristic constituent of chromosomes. Thymidine can be stably tagged with tritium. This isotope decays with the production of soft beta rays, half of which have a range (in tissue) of 1 μ or less. Accordingly, they will produce autoradiographic registration only over the labeled nucleus. It is thus possible to recognize unequivocally the nuclei of cells that were synthesizing DNA at the time the label was administered. With this method, the position of cells in S phase can be identified, and the rate of synthesis roughly estimated. The subsequent fate of S phase cells can be studied by sacrificing animals at various times after labeling (see Fig. 1).

It is well known that irradiation affects DNA synthesis (4). With modern methods it has been possible to identify definitely three radiation effects associated with DNA synthesis: inhibition of DNA synthesis in progress (7), delay of commencement of the S phase (5), and synthesis of abnormal amounts of DNA (7). Two other effects are suspected: delay of termination of the S phase (6) and synthesis of qualitatively abnormal DNA. These effects are not necessarily primary biochemical lesions.

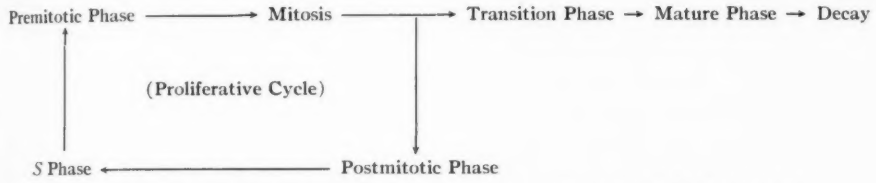

Fig. 2. Phases of cell proliferation and renewal in the intestinal epithelial cells of rodents.

RADIATION EFFECTS ON PHASE SEQUENCE

By combining several experimental methods, various phases associated with cell proliferation and renewal can be recognized. In a system which has been intensively studied, the intestinal epithelium of rodents, 7 distinct phases of cell life have so far been identified, the orderly sequence of which is indicated in Figure 2. One of the phases, mitosis, may be succeeded by either of two different phases. (A possible third alternative is differentiation into goblet cells, but this is not relevant to the present discussion.) This nice order breaks down after irradiation. Several abnormal phase transitions have been definitely established, and several more are suspected. It might be that irradiation results in more or less complete disorganization of the phase sequence (see Table III).

The cells resulting from disorderly transitions are often—possibly always—abnormal. Two instances are of particular interest.

(*a*) *Transition from S Phase to Mature Phase: Precocious Maturation:* Irradiation (in sufficient doses) stops DNA synthesis in *S* phase cells. A few of the cells thus disturbed die, and some return to a presynthetic stage, but the vast majority mature and are transformed into villus cells. It has been shown, by varying the time relations between irradiation, labeling with tritiated thymidine, and sacrifice, that the maturation occurs before the cells have had time to complete the doubling of chromosomal material (9). Accordingly, the cells must have an abnormal, incompletely doubled, complement of DNA. They are probably irreversibly sterilized; it is most unlikely that such cells could successfully dedifferentiate. The phenomenon of increased frequency of maturation which is so important in irradiated cancers (2) is probably related to precocious maturation.

(*b*) *Transition from Premitotic into Presynthetic Phase: Increased DNA Complement:* Irradiation blocks the entry into mitosis of some (or, with high enough doses, all) cells which were in the premitotic phase at the time of irradiation. Most of these cells do not enter mitosis subsequently, but revert to a presynthetic phase which, however, differs from the normal by the fact that the chromosome material has been doubled. If such cells enter into a new *S* phase, they will come out of it with a quadruple amount of chromosome material, and a successive division will give rise to cells containing twice the normal amount of DNA. It does seem that more than one DNA-doubling phase without division can occur in irradiated cells. The resulting cells are abnormal in size and shape and presumably in function. Of particular interest is the fact that—in some cases at least—they are more radioresistant than their normal ancestors. This appears to be one mechanism of adaptation to radiation (8).

In conclusion, radiation effects on cell proliferation are manifold and complicated. Extensive studies have revealed a multiplicity of effects on mitosis; the studies of DNA synthesis, which were begun much more recently, have already revealed several distinct effects. It is therefore to be expected that additional analytical methods will bring to light still more types of damage. Moreover, analyses of the proliferative cycle as a whole have disclosed disturbances of a higher order of complexity, reactions which are characterized less by disturbance of simple functions than by upset of their normal co-ordination. Complex reactions are difficult to study and to evaluate.

Under these circumstances, there does not seem to be much hope that a simple, all-embracing relation between cell proliferation and radiosensitivity will be discovered in the future. If I may venture to predict future developments, I would expect that the complex effects—exemplified by the disorganization of phase sequence—will prove to be the most important ones. It may not be useless to speculate on therapeutic utilizations of complex effects.

SUMMARY

The relations between radiosensitivity and cell proliferation are complex. Not all proliferating systems are radiosensitive; neither are all radiosensitive systems proliferating. Two phases of cell proliferation are known in some detail: mitosis and chromosome doubling. Both are affected by irradiation in a variety of ways. In addition, irradiation upsets the normal sequence of phases of cell life, and this disturbance leads to a variety of secondary effects.

Brookhaven National Laboratory
Upton, L. I., N. Y.

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SUMMARIO IN INTERLINGUA

Renovation de Cellulas e Acute Vulneration Irradiatori

Le differentias in le radiosensibilitate de differente cellulas es non solmente de interesse per se; illos es etiam de importantia ab le puncto de vista del radiotherapeuta qui debe prender in consideration le differentias in sensibilitate inter cellulas cancerose e le circumjacente histos normal. Multe sed non omne radiosensibile systemas cellular es systemas proliferante, e multe sed non omne proliferante systemas cellular es systemas radiosensibile.

Mitose es un aspecto conspicue de proliferation, e al minus novem effectos del radiation super iste processo pote esser distinguite: Adhesivitate del chromosomas; retardo de mitose; fracturas, pontes, e fragmentos; mitose pluripolar; imbalancia genic post le mitose; abortion de cellulas durante o post le mitose; division de chromosomas sin division nuclear; division nuclear con division cellular; e division cellular sequite per fusion.

Irradiation etiam inhibi le synthese de acido disoxyribonucleic jam in progresso, retarda le comenciamento del si-appellate phase S (durante le qual le cellula sinthetisa nove material chromosomal), e causa le synthese de quantitates anormal de acido disoxyribonucleic.

In plus, le cyclo proliferative in su integritate es afficite con le resultato de alterationes de un alte ordine de complexitate, characterisate minus per disturbation de simple functiones que per le confusion de lor coordination normal.

The Effect of Combined Irradiation and Chemotherapy on Cancer Growth

With Special Reference to Studies with Folic Acid Analogues[1]

MERLE K. LOKEN, Ph.D., YOUNG S. KIM, M.D., DONN G. MOSSER, M.D., and JAMES F. MARVIN, Ph.D.

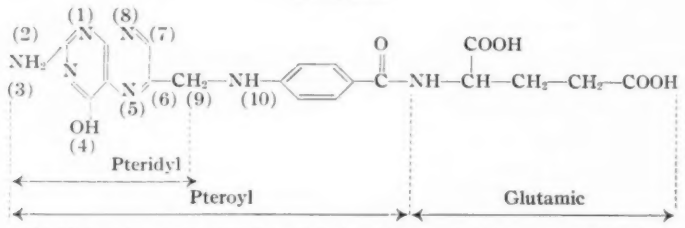
DURING THE PAST four years we have been investigating the effects of chemicals on the radiation sensitivity of various biological systems. Particular emphasis has been given to the study of combined chemical and radiation therapy in the treatment of cancer. Chemical compounds which have been used include various porphyrins, folic acid analogues, sulfhydryl compounds, cortisone, sodium cyanide, and di-chlorovinyl-cysteine (1–4). Of these, the folic acid analogues have received special attention (5, 6) and are the subject of this report.

By combining chemical and radiation therapy it may be possible to increase "therapeutic ratio," which has been defined as the ratio of the radiosensitivity of tumor tissue relative to surrounding normal tissue (7). If the therapeutic ratio can be increased by chemical means, it would be possible to deliver a cancericidal dose of radiation with less damage to normal tissue. This may be accomplished either by sensitizing tumors to the effects of x-rays or by preferential protection of normal tissues.

One reason for expecting synergistic action of certain chemicals and radiation in the treatment of malignant tumors is evidence that alternate metabolic pathways exist in cells, so that blocking one path by administration of a particular chemical or by radiation therapy may not produce the desired response. However, if both a major pathway and its alternates were blocked, a specific result might be achieved, such as the inhibition of nucleic acid synthesis in tumors.

Folic acid is apparently the immediate precursor of folinic acid, which is considered to be the active form of the vitamin in most animals. Although the metabolic role of this vitamin is not completely understood, there is evidence that its functional forms are intimately associated

Folic Acid



N-[4-{[(2 amino-4-hydroxy-6-pteridyl)-methyl]-amino}-benzoyl]-glutamic acid

Folic Acid Antagonists

Aminopterin	4-amino-PGA
Methotrexate	4-amino-10 methyl-PGA
Aminoteropterin	4-aminopteroyl (glutamyl)$_2$ glutamic acid
An-Fol-A	Pteroyl aspartic acid

[1] From the Division of Radiation Therapy, University of Minnesota Hospitals, Minneapolis, Minn. This work was supported in part by grants from the Minnesota Division of the American Cancer Society and The Graduate School of the University of Minnesota and by grant CY 3332 (CL) from the Public Health Service.

Presented as part of a Symposium on Radiation Biology at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

with processes involving methylation, such as are required fo rsynthesis of purines and pyrimidines. Animals deficient in folic acid and folinic acid exhibit a decreased capacity to utilize carbon dioxide, formate, and glycine for nucleic acid synthesis.

Since the development of the first folic acid antagonist by the Lederle group in 1947 (8), for use by Farber and his associates in the clinical investigation of acute leukemia in childhood (9), the literature on this subject has become voluminous. Higgins and Woods (10) reported that aminopterin restricted the growth of transplanted mammary tumors in C_3H mice during the period of administration. The effects of either aminopterin or 6-mercaptopurine combined with radiation in the treatment of cancer have been described by Thomas (11), who reported dramatic improvement in a patient receiving this combined therapy. Limited trials on tumors in mice, however, were discouraging because of the high mortality among treated animals. Several investigators (12, 13) have demonstrated that aminopterin inhibits the growth of sarcoma 180 in mice. Taylor and Carmichael (14) have shown that this analogue causes preferential inhibition of mouse mammary tumor in embryonated eggs. Sugiura and associates (15) reported that folic acid analogues inhibited the growth of melanoma and mammary and ascites carcinoma in mice and sarcoma 39 in rats.

Inasmuch as the folic acid analogues and ionizing radiations have some similarities in their effects on biological structures, it was felt worthwhile to explore their possible synergistic action in carcinostasis. Such synergistic action, probably related to the inhibition of major and alternate metabolic pathways leading to the synthesis of nucleic acid, might eliminate the refractoriness known to develop in tumors after repeated treatment with either agent alone.

METHODS AND MATERIALS

Mice of our Z stock, weighing from 15 to 20 gm., were used in most of these studies. Male mice were used when available because of reported variations in the radiosensitivity of females depending upon the phase of estrus. However, shortages of animals necessitated the utilization of female mice in some experiments.

Strain-specific transplantable mammary carcinoma obtained originally from spontaneous mammary carcinoma in our Z stock and carried through several generations by serial transplantations was used for the tumor experiments. A volume of 0.05 c.c. of a 50 per cent tumor-saline suspension was inoculated into the dorsal aspect of the right hind leg of each of the experimental animals. When the tumors had reached 6 to 8 mm. in one dimension, the tumor-bearing animals were randomly grouped for experimentation.

The folic acid antagonists[2] were tested for possible toxic effects prior to their utilization in combined therapy experiments. Of the antagonists used, aminopterin was found to be the most toxic and was used sparingly in our work. The majority of the experiments on the effect of these analogues on tumor growth when used with radiation have involved the use of Methotrexate, An-Fol-A, and Aminoteropterin. These latter three analogues were dissolved at a concentration of 500 micrograms per milliliter of 2 per cent sodium bicarbonate. Aminopterin was normally used at one-tenth this concentration. It was found that 0.5 ml. of these solutions could be injected intraperitoneally into mice without appreciable mortality. This volume of a particular solution was administered thirty minutes prior to radiation treatment. Groups of animals receiving 2 per cent bicarbonate without any dissolved analogue were included in all experiments.

Irradiation was performed with a G.E. Maximar 220 x-ray machine. For studies involving total-body irradiation of mice, this machine was operated at 220 kvp and 15 ma, with a filter of 0.25 mm. of copper and 1.0 mm. aluminum (h.v.l., 0.95 mm.

[2] These compounds were made available to us through the courtesy of the Lederle Laboratories.

TABLE I: MORTALITY IN Z MICE RECEIVING FOLIC ACID ANTAGONISTS 30 MINUTES PRIOR TO TOTAL-BODY X-IRRADIATION

Injection	450 r			550 r	
	No. of Animals	Per Cent Mortality (30 days)	Days for 50 Per Cent Mortality	No. of Animals	Days for 50 Per Cent Mortality
Aminopterin	20	100	7	20	6
Aminoteropterin	20	70	9	20	8
Methotrexate	20	70	12	20	10
An-Fol-A	20	70	12	20	7
2 per cent sodium bicarbonate	20	60	15	20	12

copper) and a focal-skin distance of 60 cm. For irradiation, mice were placed in a Lucite box with individual compartments patterned after the unit described by Ellinger (16). This chamber was supported on 10 cm. of Presdwood to achieve full back-scatter. Under these conditions, the animals received an average skin dose of 68 r per minute as measured with a Victoreen r-meter.

For local irradiation of the tumor-bearing mice an especially built treatment cone was used, which permitted the leg to be exposed to radiation while the remainder of the animal was protected by a lead shield (17). The x-ray machine was operated at 140 kvp and 15 ma with 2.0 mm. aluminum filter (h.v.l., 0.43 mm. copper) and a focal-tumor distance of 28 cm. Under these conditions the dose rate was 150 r per minute. Animals in nonirradiated control groups were immobilized on a similar cone for the same time to eliminate any differences due to handling alone.

EXPERIMENTAL RESULTS

1. *Folic Acid Analogues and Total-Body Irradiation:* To investigate whether or not the folic acid antagonists might be expected to alter therapeutic ratio, two experiments were conducted in which mice were exposed to total-body irradiation. Two exposure doses were chosen, one of which was near the LD 50/30 and the other near LD 100/30. In the latter group particularly, a protective effect should be quite readily detectable. If the analogues were to alter therapeutic ratio, their effect might be one of protection from the lethal effects of radiation. However, if potentiation were observed, alteration of the ratio would be much less likely.

From other studies we have found that 450 r (in air) of total body radiation is close to the LD 50/30 for Z strain male mice at two months of age. Very close to 100 per cent mortality is observed following exposure of these mice to 550 r (total body). These two exposure doses were used in the present studies with the results summarized in Table I.

It is apparent that each of the analogues administered intraperitoneally thirty minutes prior to radiation exposure of 450 r has potentiated the lethal effects of x-rays. This may be observed in terms of both mortality rate and per cent mortality. Aminopterin, the most effective in this role, is also the most toxic of the group, and some of the deaths may be attributed to this agent alone. At 550 r, each of the analogues again produced a slight potentiation of the radiation effect—potentiation in terms of 50 per cent survival time, since all animals succumbed to this treatment. From these results one is not encouraged that the analogues could be of benefit in combined therapy. Only if they selectively sensitize tumors to the effects of radiation will they be of value. Consideration is given to this latter possibility in the next section.

2. *Folic Acid Analogues and Tumor Growth:* Seven experiments have been carried out in which mice bearing transplanted mammary tumors were given radiation therapy thirty minutes after an intraperitoneal injection of one of the analogues or of a 2 per cent sodium bicarbonate solution. The tumors were treated

with a total of 4,500 r fractionated into three equal parts over a five-day period. Mice receiving the bicarbonate solution with and without the addition of an analogue were included as controls. A total of 500 tumor-bearing mice were used in these experiments, which have been carried out over a three-year period. At the beginning of each experiment the tumors averaged 7 mm. in diameter. Results of studies concerned with the effects of other doses and other times of administration of radiation and analogues, and of multiple treatments will be considered in subsequent reports.

After plotting the average tumor size for each group of animals as a function of time after the initiation of each of the

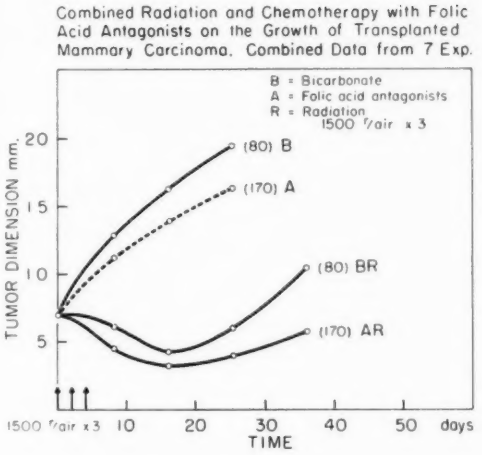


Figure 1.

TABLE II: GROWTH OF TRANSPLANTED MOUSE MAMMARY CARCINOMA FOLLOWING VARIOUS TREATMENTS

Experiment	No. of Mice	Tumor Sizes (millimeters in diameter)							
		On 16th Day				On 36th Day			
		B	BR	A	AR	B	BR	A	AR
1	100	14.2	3.8	14.2	3.8	...	10.5	...	5.6
2	80	13.6	6.1	12.1	4.9	...	11.5	...	9.4
3	40	14.5	4.0	10.5	4.9	...	10.5	...	1.0
4	100	15.8	7.5	14.2	6.0	...	10.5	...	6.9
5	60	15.8	2.4	20.9	3.8	...	8.8	...	13.3
6	60	10.0	3.4	9.7	0	...	7.7	...	1.5
7	60	26.8	1.9	21.1	0	...	11.1	...	2.6
Average size		15.8	4.2	14.6	3.4	...	10.1	...	5.7

B. Treatment with 2 per cent sodium bicarbonate.
BR. Treatment with 2 per cent sodium bicarbonate plus radiation.
A. Treatment with analogue dissolved in 2 per cent sodium bicarbonate.
AR. Treatment with analogue dissolved in 2 per cent sodium bicarbonate plus radiation.

experiments, it became apparent that groups of mice receiving the same treatment in all of the experiments exhibited a similar response. There were slight variations in the average initial tumor size from experiment to experiment so that some differences were observed in the rates of tumor regression after treatment and in the time required for the average tumor size of a particular group of mice to equal its average initial size. Because of the similarities, however, data from all experiments were combined into Figure 1, which shows the average tumor size of each experimental group as a function of time following the initiation of treatment.

A total of 170 mice received combined analogue and x-ray treatment (group AR). Tumors of this group regressed faster and remained smaller for a longer time than did tumors of the other groups. During the forty-day period of observation following the first treatment, those tumors had not regrown to an average size equaling that recorded at the start of the experiment. By the fortieth day tumors in the 80 mice treated with sodium bicarbonate and radiation (group BR) had almost doubled their initial size and in many instances were ulcerated. Furthermore, these tumors exhibited a rate of regrowth which was more rapid than that for tumors in the AR group. This is evidenced by the greater slope of the BR

TABLE III: COMPARISON OF FOLIC ACID ANALOGUES USED IN COMBINED THERAPY

Treatment	No. of Animals	Tumor Sizes (millimeters in diameter) On Days							
		4	8	12	16	21	25	30	36
MR	50	5.9	4.2	3.4	2.4	3.3	4.8	6.6	7.0
AR	30	5.7	4.8	5.2	4.4	5.2	6.2	6.9	7.0
ATR	10	5.9	4.5	4.5	4.1	3.5	4.5	4.8	4.9
AFAR	80	6.5	4.7	3.7	2.5	3.1	3.8	4.7	5.5
Average tumor size		6.0	4.5	4.2	3.4	3.8	4.5	5.7	6.1
BR	80	6.5	6.0	5.0	4.2	4.8	6.0	7.6	10.

MR. Methotrexate and radiation.
AR. Aminopterin and radiation.
ATR. Aminoteropterin and radiation.
AFAR. An-Fol-A and radiation.
BR. Bicarbonate and radiation.

TABLE IV: NONPALPABLE TUMORS FOLLOWING VARIOUS TREATMENTS

Experiment	Per Cent Nonpalpable Tumors							
	16th Day				36th Day			
	B	BR	A	AR	B	BR	A	AR
1	0	60	0	90	...	40	...	55
2	0	50	0	50	...	10	...	20
3	0	10	0	60	...	40	...	100
4	0	0	0	30	...	0	...	20
5	0	80	0	85	...	10	...	20
6	0	90	50	100	20	15	50	95
7	0	90	0	100	...	60	...	60
Average % nonpalpable	0	54.3	7.1	73.6	3.1	26.4	7.1	53.0

B. Treatment with 2 per cent sodium bicarbonate.
BR. Treatment with 2 per cent sodium bicarbonate plus radiation.
A. Treatment with analogue dissolved in 2 per cent sodium bicarbonate.
AR. Treatment with analogue dissolved in 2 per cent sodium bicarbonate plus radiation.

curve. All of the animals in the two groups treated with the bicarbonate solution, with and without the addition of an analogue, succumbed to tumor infiltration before the fortieth day. Of these two latter groups, the group treated with one of the analogues showed a slightly slower growth rate and also a slightly longer survival time. Many of the tumors in these groups began to ulcerate and become necrotic before the end of the second week following treatment.

Table II shows the average tumor size on the sixteenth and thirty-sixth day post-treatment for each of the seven experiments. Except for experiment 5, in which mice receiving bicarbonate and radiation (BR) had the smallest tumors of all groups, the tumors in the combined analogue and radiation treated groups (AR) were consistently smaller than in the other groups. In some cases the average tumor size of an AR group was increased considerably by one or two tumors which did not respond well to treatment.

The results obtained with the individual antagonists are shown in Table III. In most instances the groups of mice receiving an analogue plus radiation had smaller average tumor sizes than did the BR group. These differences became more apparent as the time between treatment and observation was increased. Except for the fourth day following treatment, the results obtained with An-Fol-A (AFAR) are slightly better than with the other analogues.

An indication of the response of tumors within each treated group of the various experiments is given in Table IV. In this table are listed the percentage of nonpalpable tumors on the sixteenth and thirty-sixth days after the initial treatment. On both of these dates the AR group showed the highest percentage of

nonpalpable tumors, this difference being more evident on the thirty-sixth day, when there were, on the average, twice as many nonpalpable tumors in the AR groups as in the BR groups. At this time no tumors were palpable in any of the animals of the AR group of experiment 3; in experiment 6, only one animal in twenty had a palpable tumor. Although many of the tumors in the BR and AR groups decreased to a nonpalpable size, the vast majority resumed growth and eventually killed the hosts. The ultimate survival of mice receiving this treatment will be reported at a later time. Survival figures through the thirty-sixth day after treatment are considered in Table V. Less than 16 per cent of those animals not receiving radiation survived to the thirty-sixth day, whereas 95 per cent of the AR and BR groups survived this same period (Table V). The average survival among AR groups was adversely affected by experiment 4, in which several mice in the AR group with relatively small tumors succumbed to what appeared to be toxic effects of the analogues.

Combined Radiation and Chemotherapy with Folic Acid Antagonists on the Growth of Transplanted Mammary Carcinoma. Effect of Different Initial Tumor Sizes.

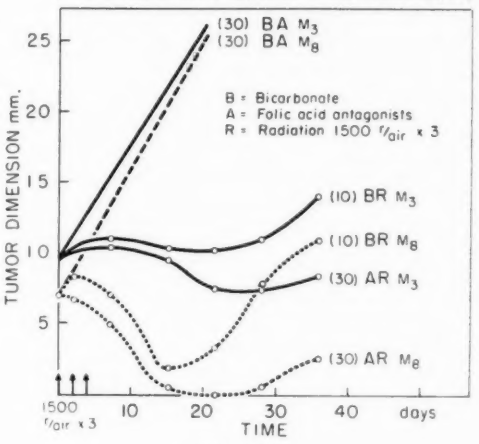


Figure 2.

TABLE V: SURVIVAL OF TUMOR-BEARING MICE FOLLOWING TREATMENT

Experiment	Per Cent Survival							
	On 16th Day				On 36th Day			
	B	BR	A	AR	B	BR	A	AR
1	70	90	60	100	0	80	0	100
2	100	100	100	100	0	90	0	97
3	30	100	60	100	0	100	10	100
4	50	100	33	92	0	100	0	75
5	75	100	85	100	0	100	0	100
6	90	100	97	93	90	100	97	93
7	80	100	80	100	0	100	0	100
Average per cent survival	70	98.6	73.6	98.0	13.0	95.7	13.3	95.0

B. Treatment with 2 per cent sodium bicarbonate.
BR. Treatment with 2 per cent sodium bicarbonate plus radiation.
A. Treatment with analogue dissolved in 2 per cent sodium bicarbonate.
AR. Treatment with analogue dissolved in 2 per cent sodium bicarbonate plus radiation.

The effect of initial tumor size on its response to treatment under the conditions of our studies is shown in Figure 2. Tumors M_3 and M_8 used in experiments 4 and 7, respectively, were treated identically in every respect. At the beginning of the experiment the average size of tumor M_3 was 9.5 mm. in diameter, whereas tumor M_8 averaged 7 mm. in diameter. Within each experiment the deviation from the mean tumor diameter was less than 1 mm.

Nonirradiated tumors in both of these studies grew rapidly, with essentially no inhibition by treatment with analogues alone. All of the animals in these groups were dead by the twenty-third day after the beginning of the experiment, indicating that tumor M_8, although smaller initially, was faster growing.

It is evident that tumor M_8 responded more readily to radiation than did tumor M_3. Furthermore, following x-ray treatment, the rate of growth of M_8 was slower. This was particularly true following combined therapy (AR), after which all tumors

in this group regressed to a nonpalpable state for almost one week. The difference in tumor size on the thirty-sixth day between the AR and BR groups was greater for tumor M_8, indicating that the smaller tumors responded more readily to combined therapy and provided more dramatic results.

It has been our experience that the more rapidly growing mammary tumors do not respond as well to radiation therapy as do slower growing tumors. Thus it seems unlikely that the differences observed in Figure 2 should be attributed to differences in metabolism as evidenced by growth rate, but rather appear to be associated with tumor size at the time of treatment.

DISCUSSION

"Therapeutic ratio," designated as the ratio of the radiosensitivity of tumor tissue relative to surrounding normal tissues, might be changed through either a preferential protection of normal tissues or by selective sensitization of tumor tissue to the effects of radiation. The latter result may be achieved either through enhancement of the direct effect of radiation on cellular components or through inhibition of recovery processes. Results of our total-body irradiation studies indicate that the folic acid analogues enhance rather than diminish the effects of radiation on normal biological structures. This constitutes a contraindication to the use of these agents for altering the therapeutic ratio.

The potentiating effect observed with the analogues in these studies may have been the result of interference with metabolic processes within the injured tissues or of blocking the synthesis of metabolites at other sites, which would normally be transported to the injured tissues. Thus the analogues might still be capable of improving the therapeutic ratio, particularly if this effect is comparatively greater in tumor tissue. Whether or not this is the case, these antimetabolites may be of definite value in combined therapy, inasmuch as the radiation is normally localized to the area involved by the malignant process.

Our approach to the study of combined therapy for the treatment of mouse mammary carcinoma has been somewhat empirical. The upper limit of doses of the analogues was dictated by toxic effects resulting in death of otherwise untreated mice. The radiation exposure dose was based on other studies which showed that doses below 4,500 roentgens were ineffective in controlling growth of mouse mammary carcinoma. The choice of a one-half hour interval between the injection of an analogue and the subsequent irradiation was quite arbitrary. It is not unlikely that a choice of other times might produce results which are actually much better.

Figure 1, which combines data from seven experiments, indicates that combined therapy (AR group) afforded a better control of tumor growth than did the other therapeutic methods used. Some of the original data from each of these experiments are shown in Table II. Except for the results obtained in experiment 5 it is evident from this table that the tumors of the groups receiving combined therapy were consistently smaller, and on the thirty-sixth day averaged about one-half the size of tumors in the BR groups. The poor response to combined therapy in experiment 5 was discouraging. It is thought that this may have been due to incomplete size randomization of the tumors. The effect of initial tumor size on its response to treatment (Fig. 2) could then account for the results. The results of experiment 5 as evidenced by the percentage of nonpalpable tumors shown in Table IV are more encouraging. On the thirty-sixth day after the experiment was started, group AR exhibited 20 per cent nonpalpable tumors as compared to 10 per cent for the BR group.

On the thirty-sixth day after the beginning of each experiment the average percentage of nonpalpable tumors in the AR group was roughly twice that observed in the BR group (Table IV). Of particular

interest are the results on the thirty-sixth day in experiments 3 and 6. In these two experiments there were about four times as many nonpalpable tumors in the AR groups as were found in the BR groups.

From Table V it is evident that the percentage survival is very much the same among the BR and AR groups. Likewise, this is comparable in the two unirradiated groups. It may be concluded from these results that the analogues alone did not produce serious toxic effects in the animals. This conclusion was also drawn from data of other studies in which weight changes were followed in animals receiving various amounts of these antagonists. It was observed that the amount of an analogue used in the experiments reported here did not seriously impair the normal growth processes in mice.

SUMMARY

Mice exposed to total body x-irradiation after administration of one of the folic acid antagonists exhibited a higher mortality rate and a higher per cent mortality than did mice which received the same treatment except for the withholding of the analogues. This enhancement of the radiation effect serves to refute the idea that the antagonists might alter therapeutic ratio. Thus the effectiveness of these agents as adjuncts in the radiotherapy of cancer might be limited.

Whether or not these analogues are capable of improving therapeutic ratio, the results of experiments using mammary carcinoma in mice indicate the potential value of combined radiation and analogue therapy in cancer treatment. Our results have indicated that tumors in mice treated with combined therapy show greater regression, remain smaller for a longer period of time, and exhibit a slower rate of regrowth than do comparable tumors treated with radiation alone.

Further improvement in the results of combined therapy is quite possible. Attention will be given in future studies to: (*a*) use of other metabolic antagonists and combinations of these antagonists; (*b*) administered dose of the antimetabolites; (*c*) exposure dose of radiation to the tumors; (*d*) time relationship between administration of the antagonists and radiation; (*e*) effect of multiple treatments; (*f*) utilization of tumors other than mouse mammary carcinoma.

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SUMMARIO IN INTERLINGUA

Le Effecto del Combination de Irradiation con Chimotherapia Super le Crescentia de Cancere, con Referentias Special a Studios con Analogos de Acido Folic

Muses exponite a roentgeno-irradiation del corpore integre post le administration de un del antagonistas de acido folic exhibiva un plus alte mortalitate que muses similemente tractate con le exception que illos non recipeva le analogos. Iste promotion del effecto del radiation servi a refutar le idea que le antagonistas es possibilemente capace a alterar le valor del nivello therapeutic. Il seque que le efficacia de iste agentes como adjunctos del radiotherapia de cancere es possibilemente restringite.

Si o non iste analogos es capace a meliorar le valor del nivello therapeutic, le resultatos del experimentos in le uso de carcinoma mammari in muses indica le valor potential de un therapia combinate de radiation e analogos in le tractamento de cancere. Le resultatos obtenite indica que tumores in muses tractate con un therapia combinate monstra plus alte grados de regression, remane micre durante plus longe periodos de tempore, e exhibi un plus lente recrescentia que tumores comparabile que es tractate con radiation sol.

Le antagonistas usate include Aminopterina (usate sparsemente a causa de su alte toxicitate), Methotrexato, An-Fol-A, e Aminoteropterina.

Potentiation of X-Ray Effects by Actinomycin D[1]

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X-RAY EFFECTS on normal tissues have been enhanced by combining roentgen irradiation with the intravenous administration of actinomycin D (1, 2), an antibiotic and carcinolytic agent isolated by Waksman (3, 4). Encouraging responses to this form of combined therapy have also been noted in a variety of neoplasms (1). One hundred and twenty-six children and adults have received 220 courses of this form of treatment at The Children's Cancer Research Foundation of The Children's Medical Center in Boston. The clinical observations to be described are based on experience with these patients.

The effects of combined therapy on normal tissues are:

1. Early erythema in the therapy portal after skin doses (including exit dose) of 350 r or less. Comparable responses after irradiation alone usually require skin doses of about 1,200 r.

2. Similar enhanced responses are obtained in the buccal and pharyngeal mucosa of patients receiving x-ray treatment to the head and neck.

3. The time required for progression of these radiation reactions in the skin through the usual stages of erythema, tanning, desquamation, and complete healing is reduced to four to six weeks rather than the two to three months usually elapsing following x-ray alone.

4. Actinomycin D therapy alone can reactivate "latent" radiation effects in normal tissues. For example, in skin previously irradiated but normal in appearance an erythema may develop during actinomycin D therapy, identical in type to that produced by roentgen irradiation. This response is sharply restricted to the areas previously treated by x-rays. The severity of the reaction varies from a mild reddening to pronounced desquamation. It is most accentuated when only a brief interval separates the courses of radiotherapy and chemotherapy.

5. These enhanced effects can lead to dangerously severe local reactions if high doses of each agent are used together or successively, or should a patient prove to be especially sensitive to the combination.

In order to study these reactions further, the effects of combined treatment on the skin of normal mice were examined. Groups of normal healthy CAF mice, approximately 20 gm. in weight, were selected. Actinomycin D was given intravenously or intraperitoneally in single doses of 150 μg./kg. or in similar amounts daily for three days. The radiation factors were: 250 kv (constant potential), 15 ma, 40 cm. T.S.D., 1 mm. Al (added filtration), h.v.l. 0.63 mm. of copper. The output at 40 cm. was 247 r per minute. The animals were shielded from the direct beam and from back-scatter by appropriate lead, only the right rear legs being included in the beam. The doses given were 1,000 r (air) in one exposure or 1,200 r (air) in three days (400 r daily).

The following observations were made:

1. There were no pathological changes produced in the skin of mice receiving only actinomycin D.

2. Earlier and more consistent epilation appeared in mice treated with x-rays combined with actinomycin D than in those treated only with x-rays. In a typical experiment, 4 of 5 mice exposed to 1,000 r plus one injection of actinomycin D showed well defined epilation nine to twelve days after irradiation, while in only 1 of 5 receiving irradiation alone did comparable epilation develop, twenty days being required for the change.

[1] From the Department of Radiology and The Children's Cancer Research Foundation, The Children's Medical Center, and the Departments of Radiology and Pathology, Harvard Medical School, Boston, Mass. This investigation was supported in part by a grant from the National Institutes of Health, USPHS #CY3335.
Presented as part of a Symposium on Radiation Biology at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

3. The changes described occurred independently of the route of administration of actinomycin D, whether intravenous or intraperitoneal. The latter method, however, seemed to be more effective, since epilation resulted in a greater percentage of the mice so treated.

4. No differences in response to combined treatment were noted in a series of experiments where x-irradiation was given: (*a*) six hours before the administration of actinomycin D; (*b*) simultaneously (*i.e.*, within one-half hour); (*c*) six hours after administration.

5. Histologic observations on skin of mice treated with combination procedures confirmed the gross changes noted. All combined therapy groups, despite variations in timing, gave a similar picture after a period of six weeks. The injurious effects sustained by these animals were qualitatively similar, consisting primarily of epilation.

6. The changes were more uniform and more accentuated in those receiving combination therapy than in those subjected to irradiation only.

Since normal tissues respond in a relatively predictable manner to irradiation, they provide a more reliable basis on which to assess possible potentiators of x-radiation. However, there are many difficulties encountered in an objective evaluation of enhancement of x-ray effects on neoplasms. Reports of synergistic action often are subjective estimates of what might have been expected after radiotherapy alone. Individuals vary in their response to irradiation, as do histologically similar tumors, so that analysis in these terms is not easy. Thus, while an augmented effect on normal tissues by combined actinomycin D and x-ray treatment has been established, a like response of neoplastic tissues is less readily documented. In our experience to date, however, these observations have been made:

1. Some neoplasms, such as the malignant melanoma, usually considered to be radioresistant, have responded well to combined therapy in some individuals.

2. The most favorable responses have been obtained in patients with Wilms' tumor, Ewing's tumor, hemangioendotheliosarcoma, and rhabdomyosarcoma, definite improvement resulting after about 75 per cent of the courses of combined therapy given to these persons.

3. Simultaneous chemotherapy and radiotherapy in low dosage appears to be as effective as higher doses of either modality alone in certain instances.

4. There is some evidence for a longer-lasting beneficial effect with combined therapy.

5. There is no apparent "cross resistance" between the two forms of therapy, even though it would appear that there is some gross similarity between some of their methods of action.

6. Neoplasms develop a resistance to the combination of agents after which they are also refractory to either one alone.

7. Potentiation of x-ray effects in normal tissues has not limited the total amount of roentgen therapy that could be given to any patient. Interruptions to allow recovery, however, have not been infrequent.

8. Striking effects have been obtained in tumors without apparent enhanced reactions in the skin or mucous membranes.

9. Conversely, the augmentation of response in normal structures has not always been accompanied by a similar potentiation in the underlying neoplasm. However, in most instances, a favorable therapeutic ratio has been preserved.

SUMMARY

Radiation responses in normal tissues and certain malignant tumors are enhanced when roentgen irradiation is combined with the intravenous administration of actinomycin D. Normal structures react after smaller doses of radiation than are ordinarily required to produce a like effect, and the healing processes thereafter proceed at a more rapid rate. Actinomycin D alone can reactivate latent radiation effects in tissues which have been previously irradiated but have returned to normal in appearance. The reaction grossly is identical

in type and distribution to that produced by the radiotherapy given earlier.

Certain neoplasms—some of them notoriously radioresistant, such as malignant melanoma—have shown a favorable response to combined therapy.

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SUMMARIO IN INTERLINGUA

Potentiation del Effectos de Radios X per le Uso de Actinomycina D

Le responsa a irradiation in histos normal e in certe tumores maligne es reinfortiate quando le irradiation roentgen es combinate con le administration intravenose de Actinomycina D. Structuras normal reage alora post plus basse doses de radiation e le processos resanatori es plus rapide. Actinomycina D sol pote re-activar latente effectos de radiation in histos que ha retornate a un apparentia normal post previe administrationes de irradiation. Iste reaction es grossiermente identic in typo e distribution al previe reaction.

Certe neoplasmas—incluse alicunes que es notoriemente radioresistente, como per exemplo melanomas maligne—ha monstrate un responsa favorabile al uso del therapia combinate.

Modification of Late Radiation Injury with L-Triiodothyronine

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With the Technical Assistance of Ralston R. Fillmore, B.S.

In 1895, ROENTGEN reported a new form of radiation. In 1896 Becquerel discovered radioactivity. In 1896 also the first cases of radiation dermatitis and epilation were observed (1). By 1902 radiation-induced cancer was reported (2). By 1910 the histopathology of late radiation changes had been documented (3).

Each organ or tissue has been shown to have a characteristic pattern of structural and functional alterations which are produced as a late effect of exposure to ionizing radiation (4). These changes appear to be related to early injury to the vascular structures and to connective-tissue elements. This in itself may produce secondary changes in the parenchymal cell of the organ in question. In addition, the parenchymal cell may be injured directly by the ionizing radiation. The interplay of these two mechanisms, and doubtless others as yet unappreciated, results in altered structure and altered ability to perform a normal role in the economy of the body. These changes do not appear to reach a static state even at times far removed from the initial injury. It would appear, therefore, that the process is a dynamic one. Attempts to understand its mechanisms may lead to methods capable of perturbing the balance. Obviously, as clinicians we are interested in exploiting those methods which would result in a return to or toward normal.

Attempts to alter the damage produced by ionizing radiation at the time it is initiated have included measures taken before and during irradiation. Attempts to modify established damage have for the most part been confined to a period of thirty days after exposure. With the exception of splenic and bone marrow transplants and their variants, no agent as yet has been found which, if given after irradiation, will modify radiation damage materially. The presence of such agents as cysteine, glutathione, cystamine, and AET at the time of irradiation appears to be necessary (5). There is some evidence that most of these protect against only one facet of the postirradiation syndrome, *i.e.*, the causes of death from the ninth to the thirtieth day. Mice so protected may have a decreased life span. Renal pathology appears to be the most frequent cause of death in these initially protected animals (6).

Attempts to alter established damage in patients have been sporadic and frustrating. Supportive measures such as transfusion for aplastic anemia or removal of severely damaged skin and underlying tissues followed by skin grafting are fairly routine. ACTH and cortisone were studied at one time because of their known suppressive effect on connective-tissue reaction to other injurious stimuli, with the hope that this effect might also be seen after irradiation. Unfortunately neither the animal experiments of Karnofsky (7) nor the human studies of Chu *et al.* (8) afforded any detectable evidence of beneficial effect.

Initially it was noted by members of our group, in patients with carcinoma of the thyroid who had severe radiation change of the skin and subcutaneous tissues, that the production of hyperthyroidism seemed to produce a beneficial effect on the postirradiation changes. This report will deal with a clinical study which was initiated in 1953 to explore the role of exogenous

[1] From the Departments of Medicine and Radiotherapy, Memorial Center, and the Section on Radiobiology of the Division of Experimental Pathology and the Division of Clinical Investigation, Sloan-Kettering Institute, New York, N. Y.

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thyroid hormones in the management of established radiation damage; 3,5,3′-L-triiodothyronine was selected for this study because of the rapidity of action of the drug as well as the promptness with which it is excreted by the body. Seventy-five patients have been followed in the radiation damage clinic in the intervening years.

METHODS

Double-Blind Study: Because of the difficulties involved in the evaluation of late radiation changes, it became apparent that a double-blind study would be necessary. For the last two years patients treated in our clinic have been assigned to drug or placebo by a prearranged statistical method. The attending physicians were not aware which patients received active material and which received placebo. Patients who were considered failures after one year were reassigned to a new form of drug, again by prearranged statistical methods.[2]

Instruments and Criteria of Evaluation: A second problem in the evaluation of the changes in the post-irradiation areas soon emerged. This was the necessity of quantitatively evaluating skin and subcutaneous tissue changes (see Fig. 1). To measure elasticity of the overlying skin a "Starrett" elasticity meter was adapted as a "pinchmeter" (F). After a small amount of practice this instrument was found to give satisfactory, reproducible results. A soft wheel planometer (D) was built to measure the circumferences of the lesions. Furthermore, a tensometer (C and E) was designed to measure the resilience of subcutaneous tissue. On one arm of this instrument a known force downward is applied; the movement of a free moving second arm represents the resilience of the underlying tissue. Springs of various tensile indices can be used interchangeably (G). Again, with a small amount of practice highly reproducible results can be obtained. Arthrometers, tape measures, and rulers were also found to be indispensable (A and B).

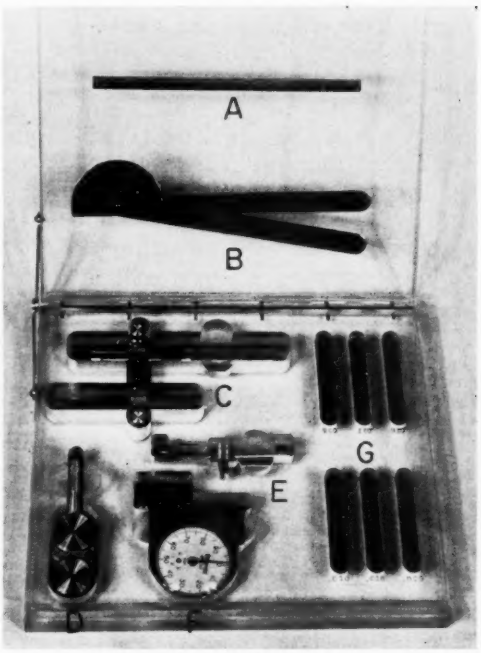


Fig. 1. Instruments used in evaluation of post-irradiation changes: A. Ruler. B. Arthrometer. C. "Tensometer." D. Soft wheel planometer. E. Rotation adaptor for "tensometer." F. Starrett pinchometer. G. Springs for "tensometer."

It was necessary, also, to define explicitly the categories into which the alteration of the late radiation changes would fall. Patients with complete healing of an ulcer or complete reversal of fibrosis were considered to have shown an *excellent* response to the drug. Those patients who had steady, progressive healing of an ulcer, or who had a minimal amount of residual fibrosis were classified as having a *good* response. Patients with somewhat slower healing of ulcers or more residual fibrosis were considered to fall into the *fair* category. Those patients who appeared to be unaffected by the addition of the drug were listed as showing *no change*. If there seemed to be an acceleration of the breakdown of the irradiated area under the influence of the drug, the pa-

[2] The authors wish to express their indebtedness to Dr. S. M. Free, head of the Statistics Section of the Research and Development Division of Smith, Kline and French Laboratories, Philadelphia, Penna., for assistance in the development of the double-blind code.

tients were classified as *worse*, due to medication.

A certain number of patients were unavailable for evaluation at the time this report was made. In some cases residual or recurrent neoplastic disease became apparent and the patients were therefore returned to the primary therapeutic service responsible for their care. In other cases, surgical intervention resulted in either partial or complete removal of the areas used for evaluation of the effect of the drug. Thirdly, because of the "double-blind" study, approximately 10 per cent of the patients received placebo medication. These patients are currently on active material but the time is too short for evaluation of effect. All these patients have been classified as *lost* to evaluation at this time.

Dosage Schedules: 3,5,3′-L-triiodothyronine (T-3) has been found to be one of the active components of the galaxy of thyroid hormones (9). Approximately 50 μg. has been sufficient to maintain an athyreotic individual in a euthyroid state. In the treatment of late radiation changes it was found necessary to administer doses between 150 and 200 μg. daily to achieve satisfactory results. To reach this relatively pharmacological dose of exogenous triiodothyronine, it was necessary to screen the patients carefully and to follow them at frequent intervals.

After a careful history and thorough physical examination, baseline biochemical studies were performed, including determinations of protein-bound iodine, basal metabolic rate, cholesterol, and esters. A complete blood count was made, and for patients over the age of forty-five electrocardiograms were obtained routinely. In any patient with evidence of pulmonary emphysema and/or fibrosis, or who was being studied for pulmonary fibrosis *per se*, pulmonary function studies were done.

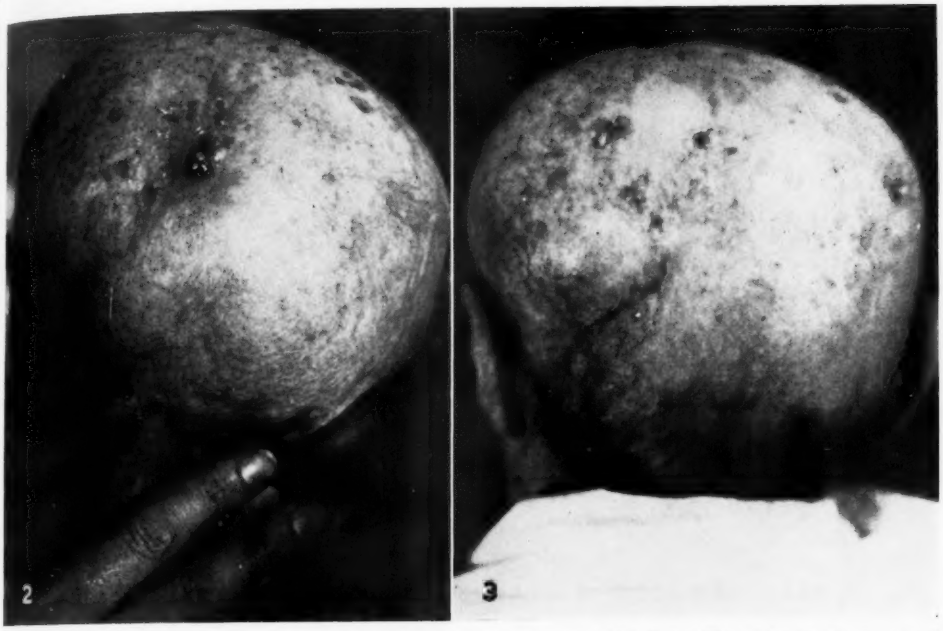
The patients were started on 25 μg. of 3,5,3′-L-triiodothyronine twice a day. One week later, if this dose was well tolerated, the amount was increased to 25 μg. three times a day. At the end of another week, if the patient showed no evidence of intolerance to the drug, the dosage was raised to 50 μg. twice daily and he was seen two weeks later. If there were still no signs of intolerance, a further increase was made to 50 μg. three times a day for ten days and then to 100 μg. twice a day for the remainder of treatment. Patients were seen with each change in dosage level. Weight, pulse, and blood pressure were checked and physical examinations were routinely performed at each visit.

If undesirable side effects such as tachycardia, excitability, headache, and excessive sweating were observed, the dose was reduced to the previous tolerated level for at least two weeks. It was either maintained at that level or an attempt was made to increase it gradually to 200 μg. per day, according to clinical judgment. In this manner the highest tolerated dose was reached as the patient was acclimatized to large doses of exogenous thyroid hormones. Some patients have been carried on 200 μg. per day for over two years. Patients who were considered "poor risk patients," *i.e.*, over seventy years of age, debilitated or with evidence of coronary artery disease, were started at 12.5 μg. twice a day, with increase to the maximum tolerated dose at two- to three-week intervals.

RESULTS

In only 5 of the 75 patients started on T-3 was there evidence of drug toxicity requiring complete cessation of the medication. This is of particular significance, since these 75 patients had 81 medical problems at the time they were referred for consideration of the use of T-3.

Total number of patients	75
Persistent neoplasms	22
Medical problems	81
Cardiac	30
Hepatic	19
Renal	10
Endocrine	10
Neuropsychiatric	8
Others	4
Drug toxicity	5



Figs. 2 and 3. Case I, on admission and after three months treatment with T-3. The patient had permanent epilation from radium treatment thirty years earlier. A craniotomy had been performed six months prior to admission. The wound had not healed and there was still leakage of cerebrospinal fluid. After three months treatment with T-3 the craniotomy wound had healed (Fig. 3). Leakage of cerebrospinal fluid had ceased four weeks previously.

Hypertensive cardiovascular disease, rheumatic heart disease, and arteriosclerotic heart disease were the most frequent medical problems. Hepatic, renal, endocrine, and neuropsychiatric difficulties were frequently present. Twenty-two patients had persistent neoplasms, which became apparent during treatment. The significance of this observation is being investigated.

Table I summarizes the effects of T-3 on late post-irradiation changes in the 75 cases studied sufficiently long to warrant evaluation. There were 46 patients with ulcerations of the skin and subcutaneous tissues two to twenty years post-irradiation. Thirteen of these were not included in the final accounting. 7 because of persistent neoplasm, 2 because of surgical intervention, and 4 because at the time of this analysis they had received only placebo medication in the double-blind study. Of the remaining 33 patients, who received active drug for periods long enough to warrant evaluation, 10 showed excellent improvement, 18 good improvement, and 4 fair; 1 was made worse. Of 24 patients with late radiation fibrosis, 8 were lost to follow-up for the reasons stated above. Of the remaining 16, 4 showed an excellent response, 7 a good response, 2 fair, 3 no change.

Only 5 patients with pulmonary fibrosis

TABLE I: EFFECT OF TRIIODOTHYRONINE ON LATE POST-IRRADIATION CHANGES

Type of Change	No. of Cases	Excellent	Good	Fair	No Change	Worse	Lost
All cases	75	14	26	7	5	1	22
Ulcers	46	10	18	4	..	1	13
Fibrosis	24	4	7	2	3	..	8
Pulmonary Fibrosis	5	..	1	1	2	..	1

Excellent. Complete healing; no residual changes.
Good. Steady progressive healing; minimal residual changes persist.
Fair. Slower progressive healing; some residual changes persist.
No change. Essentially no healing or change.
Worse. Further progression of the changes.
Lost. Not available for evaluation: persistent neoplasm, surgical intervention, or on placebo in double-blind study.

have been followed for determination of the effects of T-3. This was due to the fact that it was feared that an increased oxygen demand by the tissues in the presence of inadequate alveolar ventilatory capacity might place the patient in serious jeopardy. On T-3, 1 patient showed a good response with return of maximum breathing capacity to preirradiation levels; 1 showed only a fair response, 2 showed no change, and 1 of the group was lost to follow-up.

of the operative area was continued and the patient was started on T-3 (Fig. 2). The dosage was increased to 200 μg., as previously outlined. Three months later there was complete healing of the area (Fig. 3). The cerebrospinal fluid had ceased leaking four weeks previously.

That the patient tolerated this dosage very well can be seen in the metabolic chart (Fig. 4). There was essentially no change in her weight or blood pressure. Intermittent tachycardia did, however, occur; the cholesterol fell significantly as did the protein-bound iodine. Because of the inability of this patient to co-operate, the basal metabolic rate could not be followed.

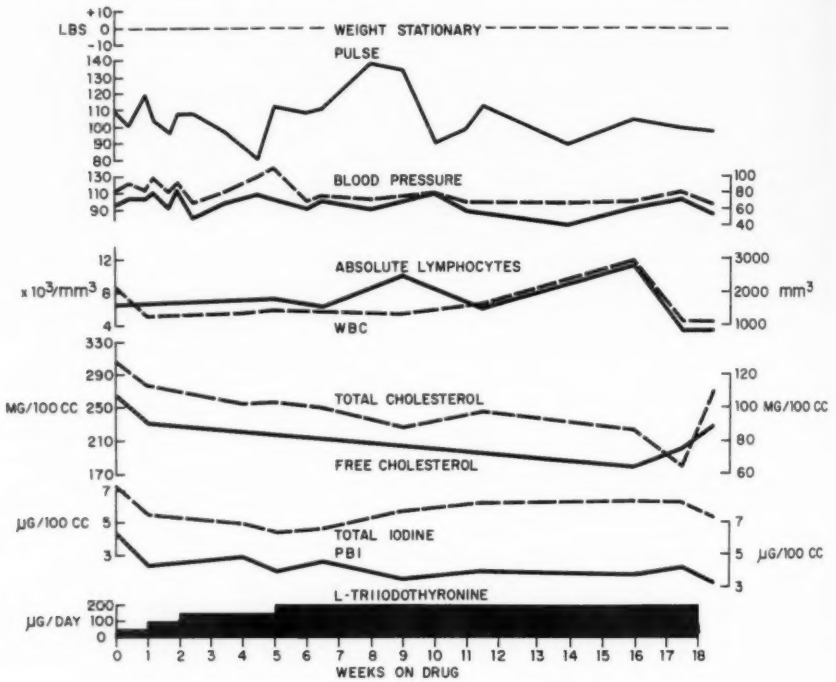


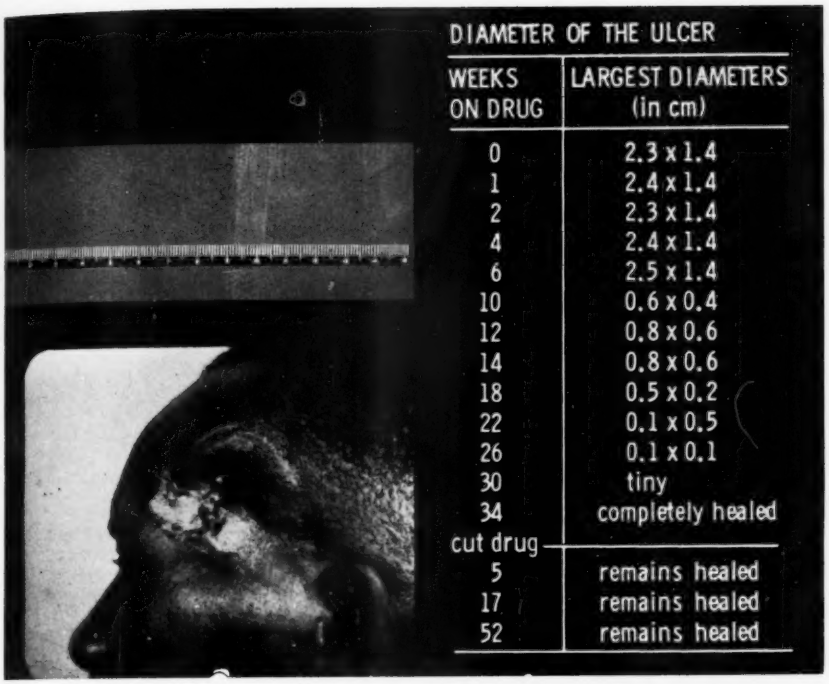
Fig. 4. Case I. Metabolic data. See text.

ILLUSTRATIVE CASES

CASE I: B. F., a 36-year-old white female, had been treated thirty years earlier in Germany, with a radium mold, for Taenia capitis. Permanent epilation resulted. Six months prior to being seen at Memorial Center the patient exhibited symptoms of an intracranial neoplasm. A craniotomy was performed at another institution, at which time a meningioma was found and partially removed. Postoperatively the scalp wounds failed to heal completely and there was leakage of cerebrospinal fluid continuously for the six-month interval. Upon transfer to Memorial Center, the routine cleansing

CASE II: C. R., 57-year-old Negro male, received radiotherapy in 1932 following surgery for a lymphangioma. For twenty-five years, he had had an almost persistent ulcer in the left temporofrontal area (Fig. 5). Attempts at skin grafting had been unsuccessful, as had routine medication and application of ointments over this period.

When the patient was started on T-3 his ulcer measured 2.3 × 1.4 cm. in its largest diameters. By the tenth week the lesion was appreciably smaller. By the twenty-second week it was almost gone and by the thirty-fourth week on the drug it was considered completely healed. In the year since the



DIAMETER OF THE ULCER	
WEEKS ON DRUG	LARGEST DIAMETERS (in cm)
0	2.3 x 1.4
1	2.4 x 1.4
2	2.3 x 1.4
4	2.4 x 1.4
6	2.5 x 1.4
10	0.6 x 0.4
12	0.8 x 0.6
14	0.8 x 0.6
18	0.5 x 0.2
22	0.1 x 0.5
26	0.1 x 0.1
30	tiny
34	completely healed
cut drug	
5	remains healed
17	remains healed
52	remains healed

Fig. 5. Case II. Left temporofrontal radiation ulcer in a man of fifty-seven, thirty years after treatment of lymphangioma.

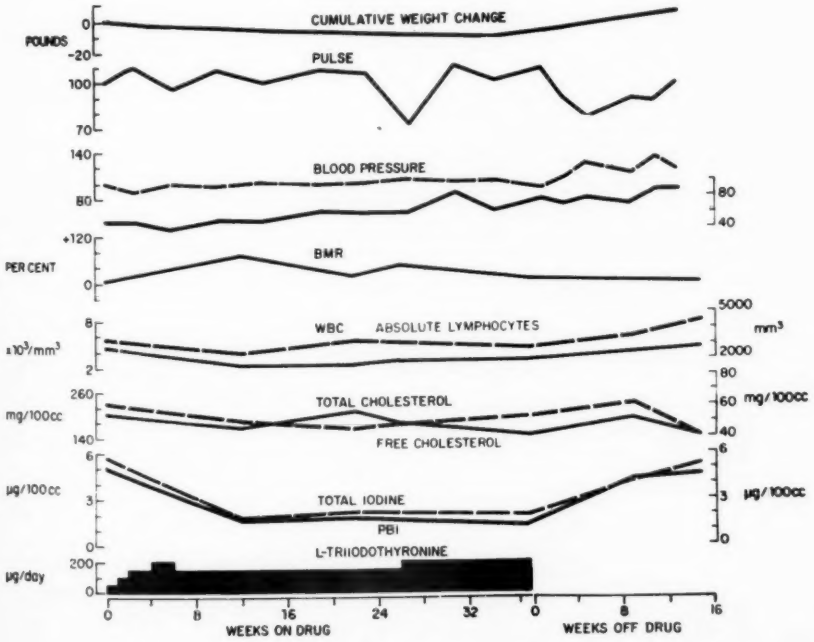
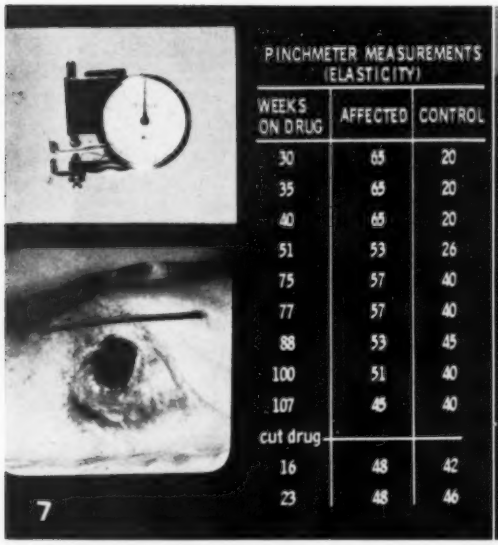


Fig. 6. Case II. Metabolic data. See text.



PINCHMETER MEASUREMENTS (ELASTICITY)

WEEKS ON DRUG	AFFECTED	CONTROL
30	65	20
35	65	20
40	65	20
51	53	26
75	57	40
77	57	40
88	53	45
100	51	40
107	45	40
cut drug		
16	48	42
23	48	46

Figs. 7 and 8. Case III. Radiation necrosis of left hip in a woman of sixty-seven (Fig. 7) twenty years after radiotherapy for carcinoma of cervix, with complete healing (Fig. 8) two years after institution of T-3 treatment and one year after discontinuance of the drug.

cessation of T-3 the lesion has remained completely healed.

The patient tolerated the drug moderately well (Fig. 6). There was an 11-pound weight loss in a period of thirty-two weeks. Basal metabolism rose to +80, and the protein-bound iodine fell to essentially 0 level. There was a small drop in cholesterol as well. The major problem, however, was the development of impotence, with only partial recovery upon cessation of the medication.

CASE III: N. M., a 67-year-old white female, received radiotherapy in 1936 for a carcinoma of the cervix. An ulceration appeared in the left hip area in 1938 which progressed so that by 1940 she could not walk at all. Attempts at skin grafting were unsuccessful. Routine cleansing, radon ointment, and other measures had also proved unsuccessful. In August 1956 the patient was completely bedridden, with a deep ulcer in the hip extending to but not including the joint capsule. At that time she was started on T-3 (Fig. 7), the dosage being progressively increased to 200 μg., which was well tolerated (Fig. 9). There was a steady, consistent weight gain despite an elevation in basal metabolic rate and a fall in protein-bound iodine. Cholesterol rose from very low levels to normal levels and remained there. There was no consistent change in blood pressure or pulse.

In approximately one year the patient showed remarkable improvement. By the second year the lesion was completely closed (Fig. 8). During this interval the patient was walking, at first with the aid of a cane and finally without any assistance.

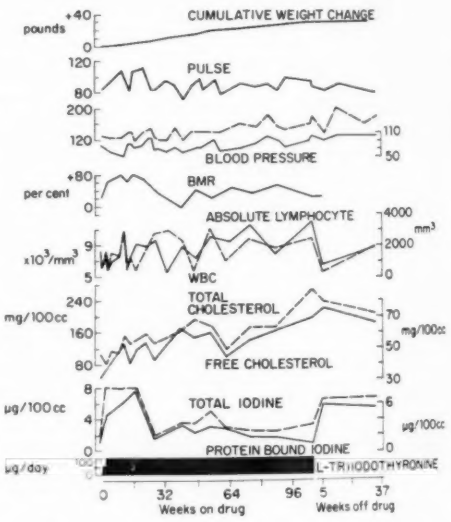
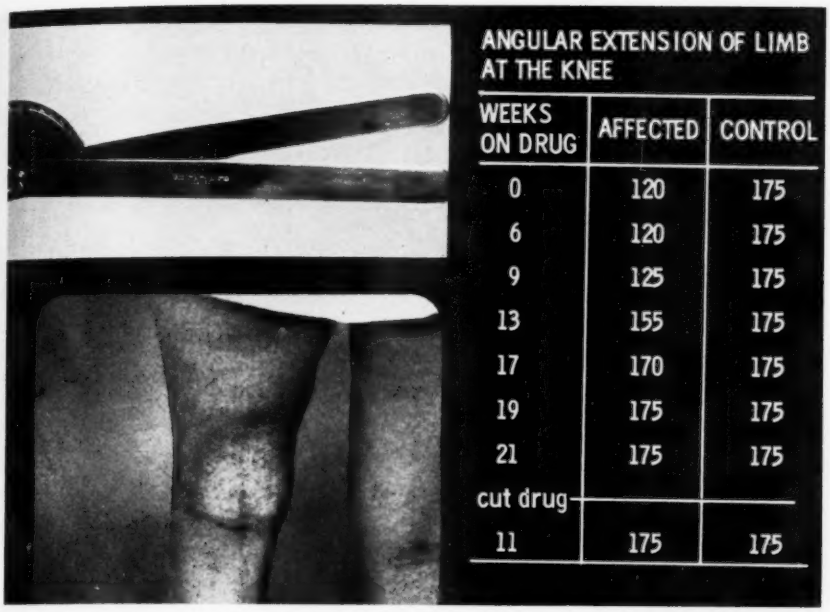


Fig. 9. Case III. Metabolic data. See text.

She is now wholly self-sufficient and in the year since medication was discontinued the lesion has remained completely healed. It is interesting to note that the "pinchmeter" measurements of the involved area of the affected side showed an increase in elasticity, while on the control side there was an increase in the resilience of the tissues. In view of the weight gain and increase in functional capacity, the changes on the control side are not surprising.



ANGULAR EXTENSION OF LIMB AT THE KNEE

WEEKS ON DRUG	AFFECTED	CONTROL
0	120	175
6	120	175
9	125	175
13	155	175
17	170	175
19	175	175
21	175	175
cut drug		
11	175	175

Fig. 10. Case IV. Fibrosis of right knee in twenty-nine-year-old woman two years post-irradiation.

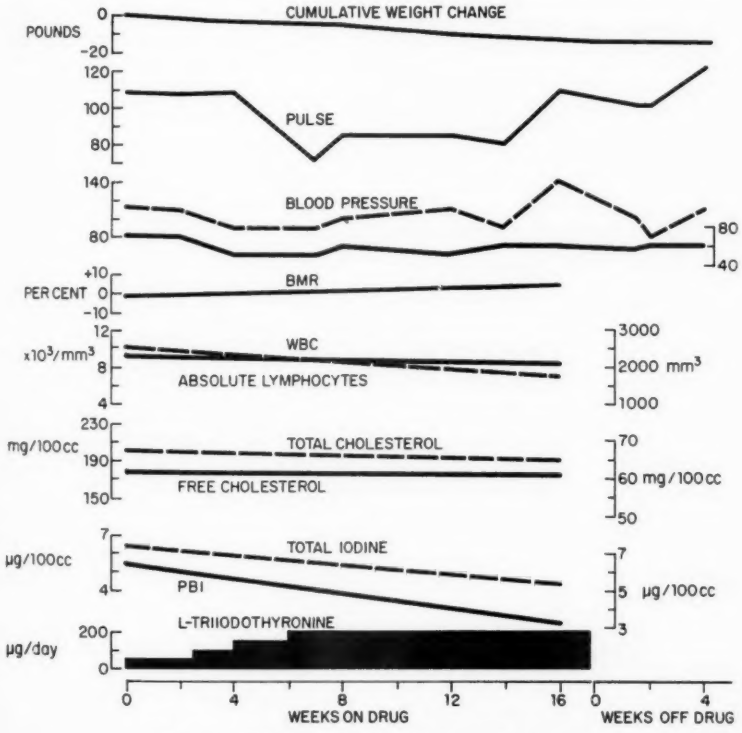
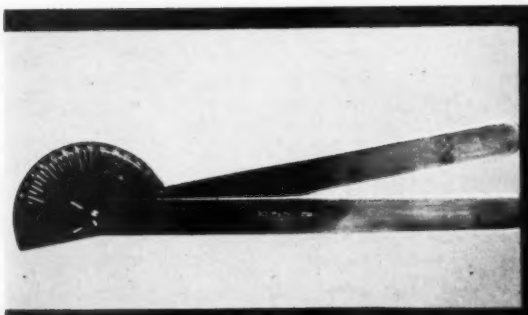
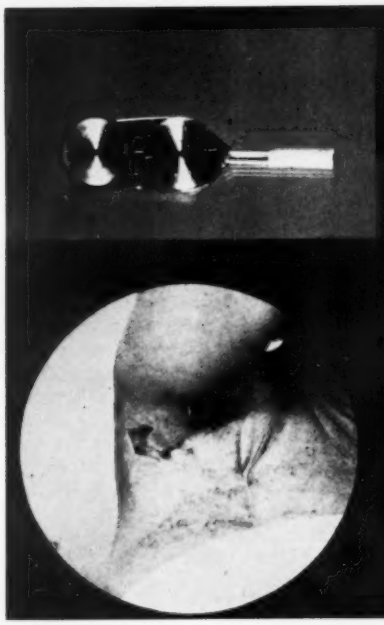


Fig. 11. Case IV. Metabolic data. See text.



ARTHROMETER MEASUREMENTS
ANGULAR ARM ABDUCTION AT
RIGHT SHOULDER

WEEKS ON DRUG	AFFECTED	CONTROL
0	85	130
5	94	130
10	85	137
15	90	135
23	90	135
31	90	135
39	90	140
47	90	135
59	90	135
64	85	135
70	85	135
cut drug		
3	85	135



EDGE CIRCUMFERENCE OF ULCER
(cm)

WEEKS ON DRUG	AXILLARY ULCER
0	19.8
5	19.5
10	16.8
15	11.5
23	10.2
31	5.0
39	11.3
47	10.0
59	11.5
64	12.1
70	12.0
cut drug	
3	11.5

Figs. 12 and 13. Case V. Radiation ulcer in right axilla, with fibrosis, two years following irradiation for carcinoma of breast. Patient on placebo. Arthrometer and planometer readings.

CASE IV: L. S., 29-year-old white female, was said in 1954, two years prior to admission to Memorial Center, to have an osteogenic sarcoma of the lower end of the right femur. This diagnosis was made at another institution on the basis of roentgenographic changes only. Information made avail-

able to us indicated that the patient had received 6,000 r to the knee joint in five weeks. A fibrosis of the knee developed, resulting in an ankylosis of the joint. The patient was referred for T-3 by the Bone Service of the Department of Surgery (Fig. 10).

After four months on the drug there was almost complete return to normal of the affected area, with improved angular extension of the limb at the knee. Three months after the drug had been discontinued there was a continuation of this improvement. The patient tolerated the exogenous hormone fairly well (Fig. 11). There was an 18-pound weight loss, which was the most serious problem. This loss continued, however, and the pulse remained elevated during the three months that the patient was followed after discontinuance of the drug. This may have been due to extraneous factors; among these were: severe financial problems and the fact that the patient was in a foreign land, in a foreign culture, and was unfamiliar with the social and dietary customs inherent in this situation.

CASE V: A. M., a 59-year-old white female, received intensive irradiation to the axilla following a simple mastectomy for carcinoma of the breast. Following a rather severe, acute moist reaction, an ulceration in the axilla developed and failed to heal in one year. The patient was then referred to Memorial Center for care. She was placed on T-3 equivalent, a placebo medication in the double-blind study. In over a year there was essentially no change in the angular abduction of the right shoulder (Fig. 12), nor was there any real healing of the ulceration, although there appeared to be an attempt at healing during the first six months of the study (Fig. 13). The wound broke down, however, and an indolent area remained for over a year on placebo medication. (The patient is now receiving a new drug and has shown some improvement after a period of three months.) It is interesting to note the variation in pulse, the elevated metabolism rate (to +40), and the changes in cholesterol and in protein-bound iodine despite the fact that the placebo was pure lactone (Fig. 14).

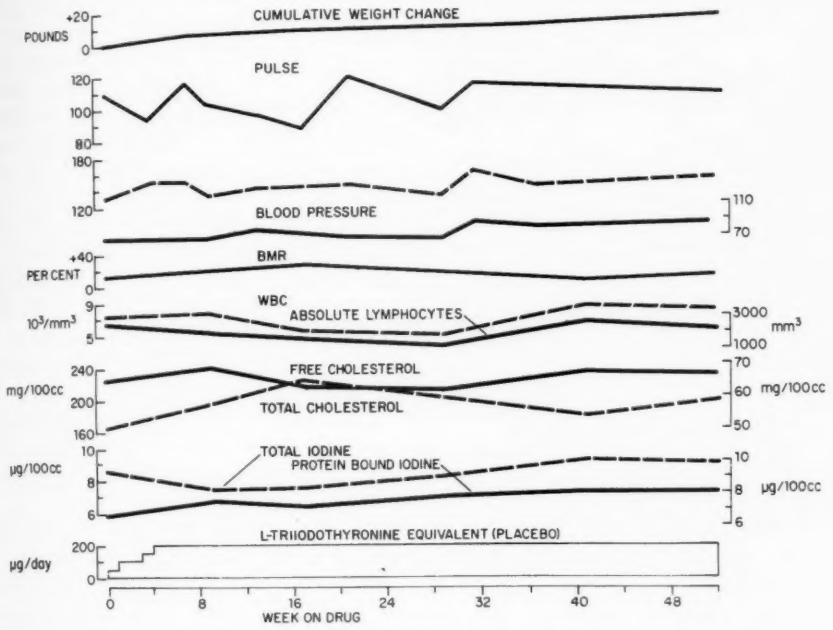


Fig. 14. Case V. Metabolic data. See text.

CASE VI: B. A., a 33-year-old white female, received radiotherapy from many physicians starting approximately twenty years earlier for acne. Seven years before admission to Memorial Center, basal-cell carcinomas around the nose and mouth were found. These were removed and plastic repair and skin grafting were performed. The major problem was telangiectasia and fibrosis, resulting in a tightening of the skin of the face (Fig. 15). The patient was placed on T-3 equivalent, a placebo medication, for a year and a half, with no appreciable change in the status of her face. During this interval, a suspicious area at the base of the nose developed and had to be removed surgically. (The patient is currently receiving active drug therapy, with no appreciable change after three months.) Fluctuations occurred in the pulse, cholesterol, and white count on placebo medication, but these ap-

Fig. 15. Case VI. Basal-cell carcinoma of face in thirty-three-year-old woman, following radiation therapy for acne twenty years earlier.

peared to be better correlated with related business anxieties than to any physiologic or pharmacologic effect of the placebo (Fig. 16).

DISCUSSION

If chronic radiation damage patterns can be modified favorably, the applicability of ionizing radiation to human disease will be broadened. At this time the cure of cancer by ionizing radiation requires the use of tolerance or near-tolerance amounts of radiation in terms of the response of the normal tissues surrounding the cancer. If this condition can be altered even slightly, two consequences emerge: decreased damage to the normal tissue, if the current time-dosage factors are preserved, or an extension of the probability of a cure by permitting the use of larger time-dosage relationships for the same degree of normal tissue damage.

These studies on L-triiodothyronine may be regarded as a progress report on a long-range effort to modify radiation damage. In our opinion, the evidence suggests that a modest but definite relief of some kinds of radiation damage can occur, and does occur, with a fair probability in so far as statistical methods are relevant to such studies. Of a series of patients with radiation damage existing for two to thirty years, well over half have shown good or excellent responses to L-triiodothyronine. Perhaps the most important thing is the demonstration that alteration of the physiologic status of the patient may improve the organism's ability to repair radiation damage. This gives solid encouragement to the search for means of improving this line of attack and continuing the pursuit of other useful leads.

L-triiodothyronine is one of the first thyroid analogues which has been shown to have physiologic activity and has been found to circulate normally in human blood. In comparatively minute amounts this compound has greater tissue metabolic effects than thyroxine. Recent studies indicate that other thyroid analogues may be developed which can separate particular tissue metabolic effects ascribed to thyroid hormone in general (10). As these new compounds evolve, it may be possible to alter the tissue metabolism in such a manner that late radiation damage will be ameliorated without production of some of the other thyroid effects. This, in effect, would remove overall drug toxicity and allow for an increase in tissue concentration of the relevant material. Currently under investigation are such compounds as triiodothyropropionic acid and triiodothyroacetic acid. These compounds, in the laboratory, have indicated a disassociation of thyroid effects such as oxygen consumption, tadpole maturation, prevention of goiter, and suppression of thyroidal avidity for I^{131}.

Laboratory studies have been undertaken which in time may lead to some understanding of mechanisms (11). It is obvious that a clear understanding of the

primary defect which is responsible for late radiation damage is, in the end, necessary. It is also obvious that no model in mammals, nor extension of any existing model, is even partially adequate for this object. Thus, both semiempirical studies such as this and laboratory studies will have to be pursued in an attempt to understand the mechanisms involved in the production of and persistence of radiation damage and the biological systems which can be affected to alter these changes.

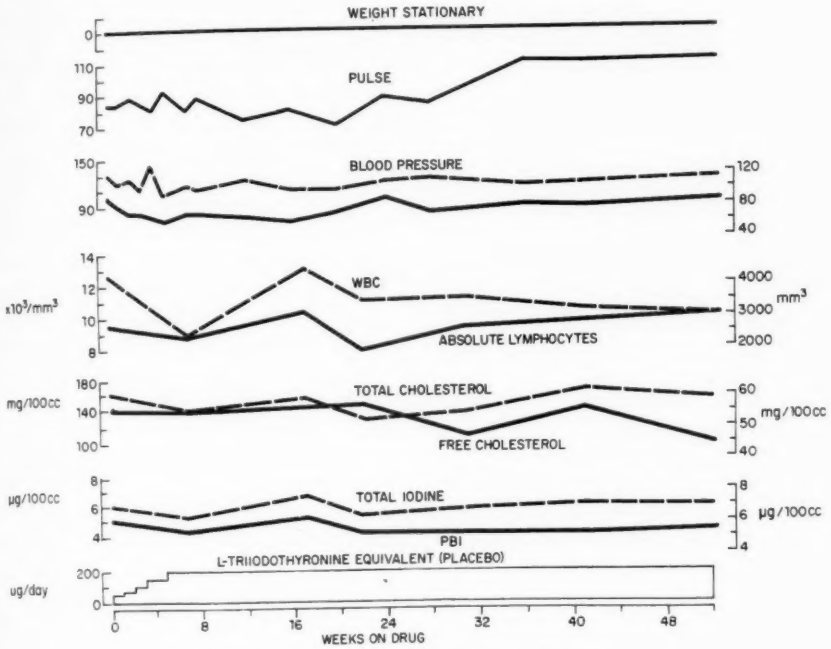


Fig. 16. Case VI. Metabolic data. See text.

CONCLUSIONS

Sixty-nine patients have been treated for sufficiently long periods to warrant evaluation of the effect of 3,5,3′-L-triiodothyronine (T-3) on established post-irradiation changes. Six patients received only placebo medication. Of the patients with damage existing from two to thirty years, well over half have shown good to excellent response to T-3 therapy. This would indicate that late radiation changes exist in a dynamic state and that it is possible to modify them by altering the metabolism of the damaged tissue.

NOTE: The 3,5,3′-L-triiodothyronine used in this study was supplied by Smith, Kline and French Laboratory Inc., Philadelphia, Penna.

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SUMMARIO IN INTERLINGUA

Modification de Tardive Injurias de Irradiation, Effectuate per Medio de L-Triiodothyronina

Un studio clinic esseva initiate in 1953 con le objectivo de determinar le rolo de exogene hormones thyroide in le tractamento de establite injuria de irradiation. Pro iste investigation, 3,5,3-triiodothyronina (T-3) esseva seligite a causa del rapiditate de su action e etiam a causa del promptitude con que illo es eliminate ab le corpore. Sexanta-novem patientes esseva tractate durante periodos sufficientemente prolongate pro permitter un evalutation del effecto de iste preparato super establite alterationes postirradiational. Sex altere patientes recipeva exclusivemente un medication fictitie.

Ex le patientes con injurias de un duration de inter duo e trenta annos, plus que un medietate monstrava un responsa favorabile al therapia con T-3. Le tractamento esseva comenciate con doses de 25 microgrammas duo vices per die, sequite per augmentos gradual—providite que nulle signos de intolerantia se disveloppava—usque a un dosage de 100 microgrammas duo vices per die. Le resultatos obtenite indica que tardive alterationes radiational existe in un stato dynamic e que il es possibile modificar iste alterationes per modificar le metabolismo del histos injuriate.

Supervoltage (2-Mvp) Rotation Irradiation of Cancer of the Bladder

MILTON FRIEDMAN, M.D.

THIS IS A PRELIMINARY report on 81 patients with cancer of the urinary bladder treated between June 1951 and June 1958 with two-million-volt x-rays by the rotation technic.

MATERIAL AND METHODS

A total of 91 patients came for supervoltage irradiation. Eleven patients were excluded from consideration in this series (Table I) because they received no irradiation. All other cases were included, whether they received "curative irradiation" or "palliative irradiation."

The patients were referred by many urologists and 75 per cent had been subjected to numerous surgical procedures of different types for successive lesions. By the time supervoltage therapy was started, most lesions were advanced, and the bladders, scarred by previous fulgurations and segmental resections and infiltrated with tumor, were not well able to tolerate intensive irradiation. Even the low-grade lesions in this series, Stages A and B_1, were extensive (Fig. 15). Thus we had the opportunity to observe the effect of supervoltage irradiation when employed as a final measure to prolong the life of patients with cancer of the bladder who were primarily treated surgically.

CLASSIFICATION

It is misleading to evaluate the comparative efficacy of a treatment technic by analyzing the total results in one group of bladder cancers. Each of the many clinical and biological types of this disease has a different prognosis and each type must be individually evaluated. Even so, no one classification encompasses all parameters satisfactorily.

The TNM system recommended by the International Union Against Cancer (1) is only partially useful, as it does not incorporate the histologic grade and type. When irradiating cancer of the bladder, we are predominantly interested in the primary tumor (T), as it is extremely unusual for a cancer of the bladder to be cured after it has metastasized to regional nodes (2). We classify primary tumors according to the Marshall (3) scatter diagram (Fig. 1). Histologic Grades 1 and 2 are papillary carcinoma; Grades 3 and 4 are infiltrating cancer. Anatomical Stage 0 is carcinoma *in situ;* A is car-

TABLE I: CARCINOMA OF THE BLADDER

(*June 1, 1951–June 1, 1958*)

Patients referred for treatment		92
Did not return for treatment	7	
Surgery advised and performed	1	
Generalized metastasis (preterminal)	3	
Patients excluded from the series		11
Net cases for analysis		81
Primary tumors	21 (25%)	
Recurrent tumors	60 (75%)	

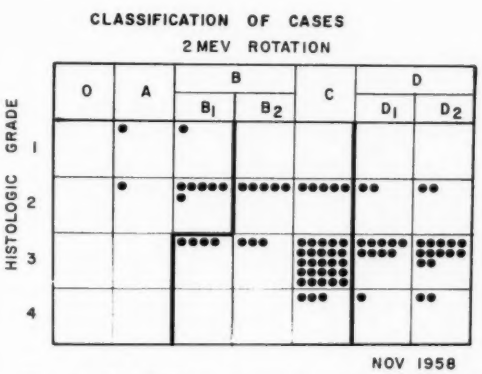

Fig. 1. Distribution of cases in this series. For further simplification the lesions have been arranged in three major groups: Early, moderately advanced, and advanced with metastasis. The heavy vertical lines subdivide these groups. The two squares, B_1—Grades 3 and 4, are included in the "early" group by Whitmore, and in the "moderately advanced" group by Rubin.

[1] From the Lila Motley Radiation Therapy Department, Hospital for Joint Diseases, and Department of Radiology, New York University College of Medicine. Presented at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

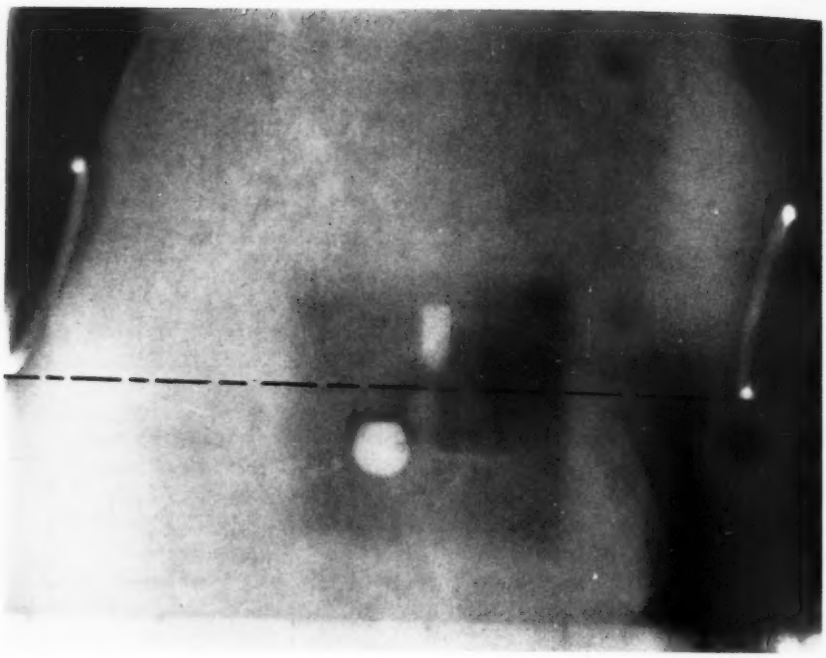

Fig. 2. Localization port film taken according to the technic indicated in Figure 3. Note the two rings on the skin surface, 5 c.c. of mercury in the Foley balloon, indicating the fixed trigone, the small ring in the upper vagina, two brass skin markers over each lateral hip, and the 50 c.c. of air in the bladder. The portal size is 8 × 8 cm. at the axis of rotation. The collapsed bladder lies in the center of the beam. The horizontal line indicates the plane along which the body contour is drawn. At the bottom of the illustration can be seen the crotch-bar notched at 5-cm. intervals for correcting the distortion factor when making measurements.

cinoma limited to the mucosa; B_1 slight infiltration of muscle; B_2 deep infiltration of muscle to the serosa; C extravesical extension; D_1 metastasis to pelvic nodes and D_2 to nodes higher in the abdomen or metastasis elsewhere.

The Marshall scatter diagram has twenty-eight categories. It would require many hundreds of cases to provide enough material in each square for analysis. For smaller series, therefore, Whitmore (4) has grouped the squares in the scatter diagram into three major subdivisions (Table IV): early lesions are 0, A, and B_1; moderately advanced are B_2 and C; advanced lesions are D. This convenient arrangement accurately expresses certain features but omits the factor of histologic degree of malignancy. Rubin (5) has modified this by shifting the more highly malignant Grades 3 and 4 of the early Stage B_1 to the moderately advanced group B_2, C. Until uniformity of reporting becomes universal, our material is presented according to Marshall's scatter diagram (Figs. 1 and 20), Whitmore's subdivision (Table IV), and also according to Rubin's modification (Figs. 1 and 15).

Many cases in this series were placed in a milder category than warranted by their actual status, because they were classified clinically by different urologists rather than after operative inspection. A number of lesions classed as Stage C probably belong to Stage D, as they undoubtedly had metastatic nodes which were not palpable or demonstrable radiographically. As a matter of fact, 40 per cent of clinical B_2 lesions are actually Stage D, according to Marshall's surgical findings (6). The experienced urologist, however, aided by

biopsy specimens from deep in the bladder wall, should be able to classify bladder cancers preoperatively with approximately 80 per cent accuracy.

In addition to the "Stage-Grade" scatter diagram classification, the lesions should be subdivided according to whether they were single or multiple, primary or recurrent. In this series, the proportion was 25 per cent primary, 75 per cent recurrent.

TECHNIC OF IRRADIATION

A two-million-volt resonant transformer x-ray generator is employed. The patient stands erect on a rotating platform during treatment. The target-axis distance is 125 cm. and the exposure dose rate at the axis of rotation is 57 rads per minute.

The technic of beam aiming is a slight amplification of that described by Trump *et al.* (8). A 5-c.c. Foley catheter is inserted into the bladder; the balloon is inflated with 5 c.c. mercury and the bladder with 50 c.c. air, and the catheter is clamped (Fig. 2). In the female, a metal ring is packed against the cervix for identification on the port film. The patient walks to the rotation platform and is strapped erect against the vertical column, from which projects a crotch bar, which he straddles. The crotch bar has two functions. It is notched every 5 cm. for correction of distortion on the film and it fixes the center of the pelvis in the axis of rotation. The right angle co-ordinate system (10) is now employed with the aid of the Dresner pointer (9). The latter eliminates the need for a cumbersome back pointer. The location of the bladder is approximated. The zero co-ordinate in the suprapubic region is identified by a metal ring fastened to the skin. This ring also is used for correction of distortion on the port film (Figs. 2 and 3). The platform is rotated 90° and a brass marker is fastened to the skin over the right hip with the point upward. The platform is then rotated 180° and another metal marker fastened over the left hip with the point downward. The posterior co-ordinate is marked with a ring.

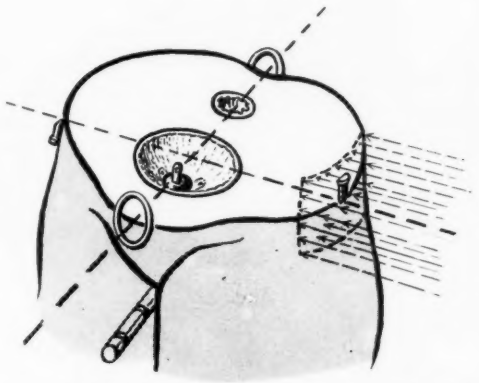

Fig. 3. Diagrammatic illustration of the technic of taking a double-exposure port film for the purpose of accurate beam aiming. Note that the anteroposterior axis goes through the center of the rings in this diagram, whereas occasionally, as in Figure 2, it goes through the bottom of the ring.

A double-exposure port film is made with an 8 × 8-cm. field at the axis of rotation. This first film almost always discloses several errors in the position of the treatment field. These are adjusted, and a second and, if necessary, a third film obtained until the direction of the beam is satisfactory (Fig. 3). The four points are painted on the skin, and all markers and catheters are removed. The body contour at this level is obtained and dosage calculations made. The port film occasionally has other uses. One can observe whether normal intestine lies in the volume of high dosage (Fig. 2).

In order to outline a mass in the cul-de-sac, a second 30-c.c. Foley catheter may be inserted in the rectum and the balloon inflated with 5 c.c. mercury and 25 c.c. air; the rectum and sigmoid are then outlined with air introduced through the main channel of the catheter (Fig. 4).

At each subsequent daily treatment, the patient is strapped to the platform and the x-ray beam aimed by aligning the Dresner pointer with the skin marks over each hip. Once or twice during the course of treatment the port film procedure is repeated to assure accuracy. There has seldom been a shift of the beam as great as 1 cm. No patient was unable to stand up for his treatments.

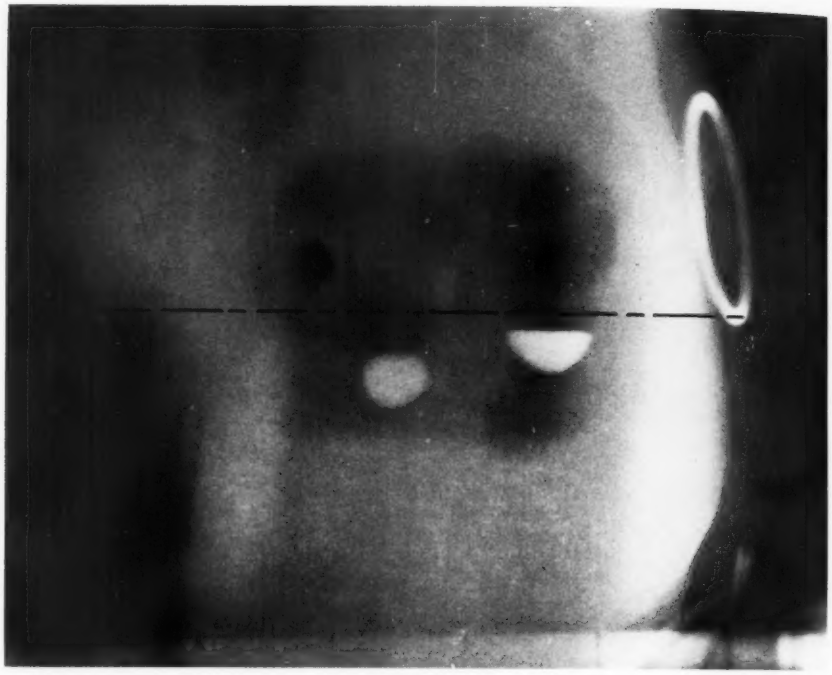

Fig. 4. Another type of port film for irradiating a carcinoma of the prostate. In addition to the usual devices for the bladder, there was inserted into this patient's rectum a 30-c.c. Foley catheter into which was injected 5 c.c. of mercury and 25 c.c. of air. Additional air was injected into the sigmoid through the central channel of the catheter.

In most instances the field size at the axis of rotation was 8 × 8 cm. Occasionally, when an advanced cancer infiltrated the pelvis, the field size was enlarged to 12 or 15 cm. in horizontal diameter. Its vertical height was rarely greater than 10 cm., because of danger of irradiation injury to the small intestine.

PHYSICAL CONSIDERATIONS

The destruction of bladder cancer requires large maximum tumor doses, ranging from 8,000 to 10,000 rads or more (Figs. 10 and 11). It is possible to deliver safely doses of this magnitude with 2-Mev x-rays and the rotation technic (10), providing the beam is well collimated in order to minimize penumbra. Good collimation is particularly important for shorter target-skin distances in cobalt teletherapy machines in order to produce distributions comparable with that in Figures 5, A and 6, A. In Figure 5, A, for example, the "index of efficiency" (*i.e.*, the distance in centimeters from the 90 per cent to the 50 per cent isodose line) (11) is 2 cm. Thus the gradient from the high-dosage tumor region to the low-dosage normal-tissue region is sharp. If the penumbra is large, due to poor collimation, the index of efficiency can be as great as 6 cm. The resultant dispersion of large dosage throughout normal tissues renders dangerous the attempt to administer the necessary large tumor-lethal doses required by a majority of bladder cancers. The 100 per cent isodose line represents the maximum tumor dose. The actual tumor dose in our series is 80 to 90 per cent of the stated 100 per cent maximum.

The nearest normal organ subjected to dangerously large amounts of radiation is the rectum. Its tolerance dose is 8,000 rads in five to nine weeks. For the rest of the

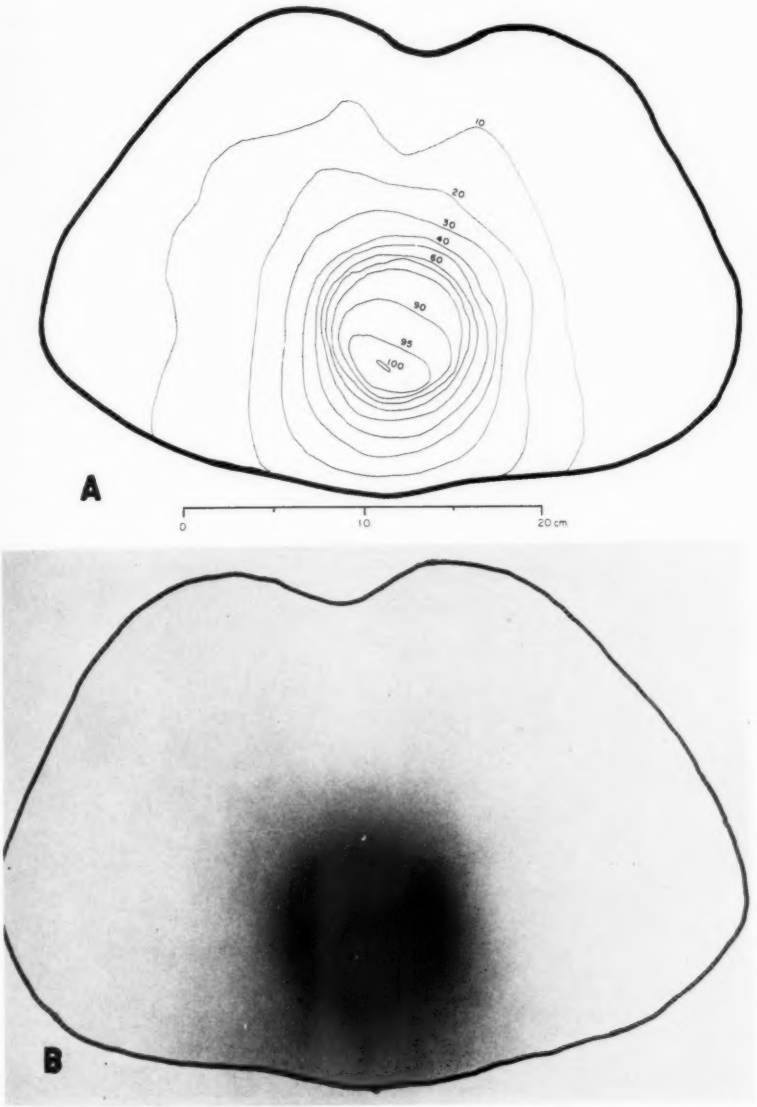

Fig. 5. A. Isodose distributions in the irradiation of a bladder cancer with 2-Mvp x-rays; 360° rotation; 8 × 8-cm. portal at the axis of rotation. The isodose curves were derived by densitometric studies from the film in B.

B. Film exposed in a masonite phantom to 2-Mvp x-rays; 360° rotation, 8 × 8-cm. portal at the axis of rotation.

intestines the tolerance dose is 4,500 rads (7). In order to spare the rectum, one might be tempted to use 180° rotation (Fig. 6, A and 6, B). This is unwise for two reasons. The tumor dose to the trigone and posterior bladder wall may be unduly reduced. The bladder is occasionally not located in the anterior part of the cross section of the patient because of abdominal wall obesity in older persons (Fig. 7).

When the diameter of the cylinder of high dosage is enlarged from 8 cm. to 15 cm. (Fig. 8), as for advanced cancer

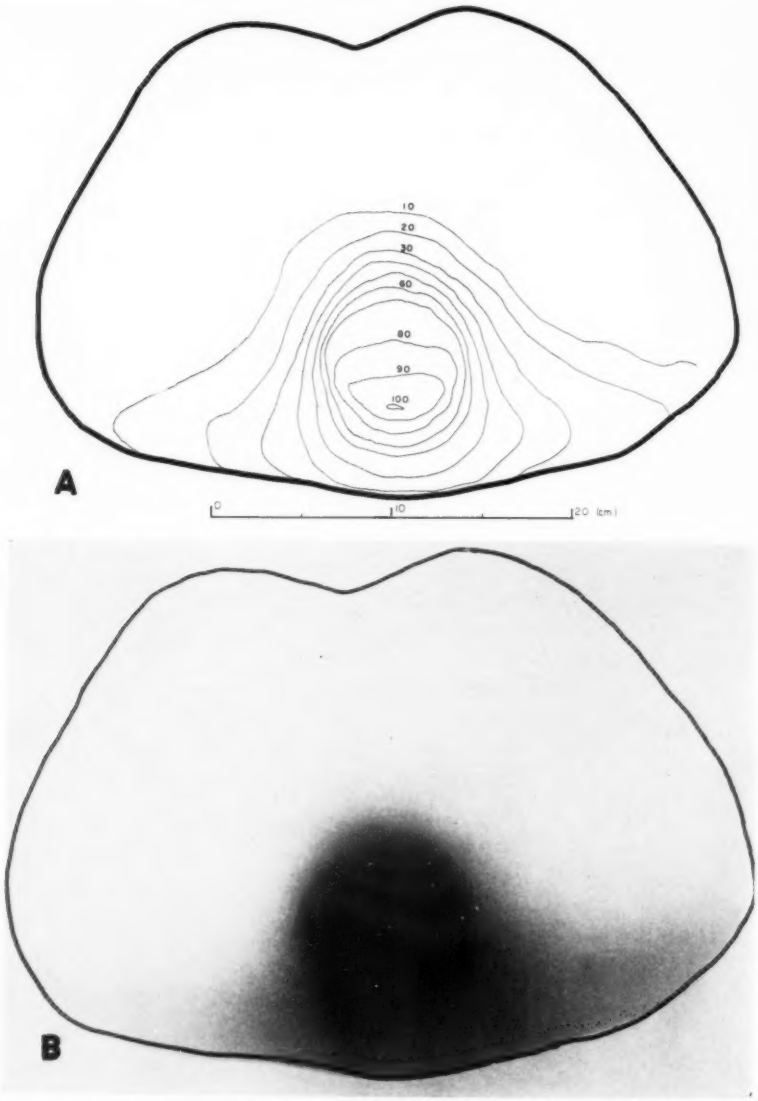

Fig. 6. A. Isodose distributions in the irradiation of a bladder cancer with 2-Mvp x-rays, 180° anterior sectoral rotation. The portal measured 8 × 8 cm. at the axis of rotation. The isodose curves were taken from the film in B.

B. Film exposed in a phantom to 2-Mvp x-rays: 180° sectoral rotation; portal size 8 × 8-cm. at the axis of rotation.

with metastasis to the pelvis, the index of efficiency is reduced from 2 to 6 cm. and the dosage to the normal tissues becomes markedly increased. Nevertheless it is still clinically possible, on occasion, to deliver tissue doses of 8,000 to 9,000 rads to the entire pelvis. Whether this is worthwhile for palliation of advanced cancer will be discussed later. In any event, as the diameter of the high dosage cylinder approaches that of the body cross section, rotation becomes progressively less efficient and finally loses any advantage over multiple portal technics.

The same principle of ratio of portal diameter to patient diameter is illustrated in a different fashion in Figure 7. In all three patients the portal width at the axis of rotation was 8 cm., but the differences in diameter of the patients changed not only the index of efficiency but also the tumor-air ratio.

The dose distribution for a central intracavitary point source (2) is illustrated in Figure 9. This is actually a picture of the effect of inverse-square law on dosage. From a central source the index of efficiency with reference to low dosage in normal tissues is excellent. There is, however, a rapid fall-off of dosage within the bladder wall. If clinical radiotherapy were dependent solely on physical dosimetry

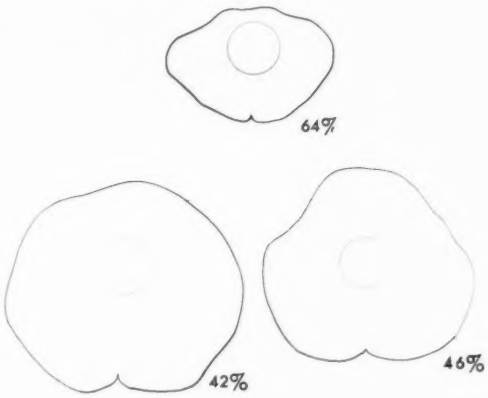

Fig. 7. Representative contours of patients with carcinoma of the bladder and their respective tumor-air ratios. Note that the bladder is not necessarily in the anterior part of the cross section of the individual

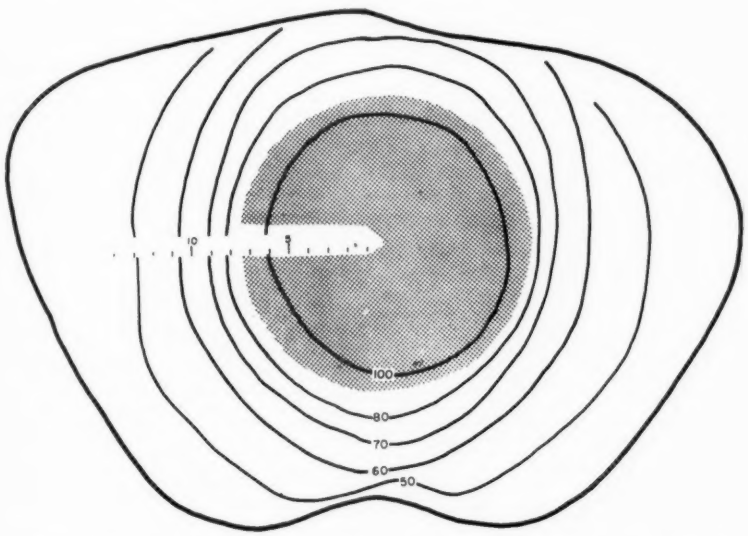

Fig. 8. Isodose distributions obtained with 2-Mvp x-rays, with 360° rotation. The portal was 15 cm. in diameter at the axis of rotation, in order that the entire pelvis might be irradiated for advanced cancer. Note that with a portal of this size the index of efficiency of the irradiation is low in that the tissue dose to the outlying normal tissues becomes very high.

considerations, the central source would be inferior to external rotation irradiation. As will be indicated later, however, use of a central source will probably cure more bladder cancers than external irradiation.

DOSAGE

The maximum stated dose required to destroy cancer of the bladder ranges from 6,000 rads in forty days to 11,000 rads in fifty-five days. The modal doses range from 8,500 to 10,000 rads. In our considerations, for the sake of constancy, we always cite the dose at the 100 per cent isodose line (Fig. 5, A) but recognize that the dose at the 90 or 80 per cent line usu-

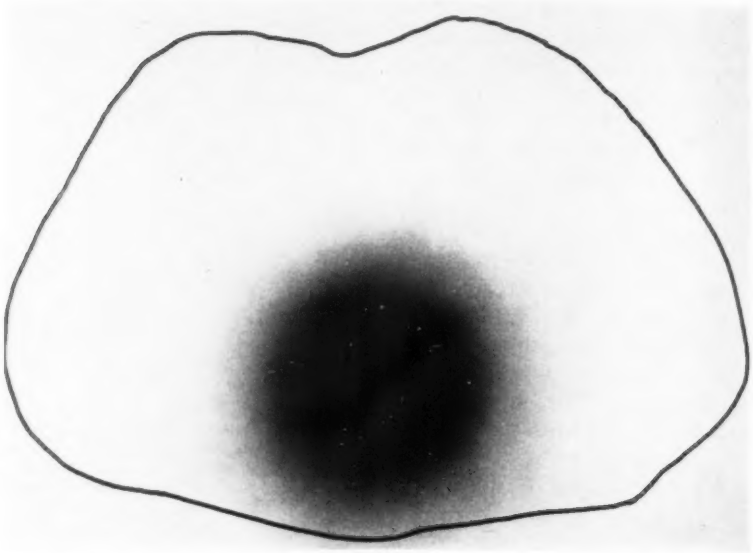

Fig. 9. Dose distribution from a central intracavitary source. This film was made by placing a minute radioactive cobalt pellet source on an x-ray film. The dose distribution is somewhat similar to that obtained with 2-Mvp x-rays in Fig. 5, B. With a central source, however, there tends to be a more rapid fall-off of dosage within the bladder wall.

ally represents the average tumor dose. Most carcinomas of the bladder are far more radioresistant than squamous-cell carcinoma of the cervix or upper respiratory tract. An occasional bladder cancer is radiosensitive and can be destroyed with a dose as low as 6,000 rads, but in our experience the routine employment of the latter dose yielded few arrests, and there were many residual cancers following larger doses (Fig. 11).

Because external irradiation of bladder cancer produces severe radiation cystitis, it is desirable to give the smallest useful dose. We are not yet able, however, to select beforehand the radiosensitive tumors which might require less than an average amount of radiation. Some early papillary cancers may respond to smaller doses (Fig. 10) than the more advanced infiltrating cancers (Fig. 11). Although one tumor was destroyed with 5,800 rads in forty-two days, nevertheless most doses for early papillary cancers ranged from 8,000 to 9,000 rads.

Each dose indicated in Figures 10 and 11 represents the amount required to destroy a particular tumor, and not to effect the cure of a patient, which depends on additional factors. Some of the dose points in the scatter diagram are true in that they represent the dose to a large recurrent mass in the bladder, pelvis, or the abdominal wall. The relative radioresistance of bladder cancer is affirmed not only by the large doses necessary to destroy some tumors, but also by the many failures to destroy a particular tumor with maximum doses as large as 9,000 to 10,000 rads.

As stated earlier, in order to be able to deliver the doses which we believe are necessary, the requirements are: high energy x-ray or gamma ray beam; a source-axis distance of at least 85 cm. (we use 125 cm.); a well collimated beam; and either precision multiple portal technic or rotation. Theoretically, a 22-Mev betatron can provide a suitable dose distribution when only four portals are employed. It remains to be demonstrated clinically whether this simple technic can arrest a significant per-

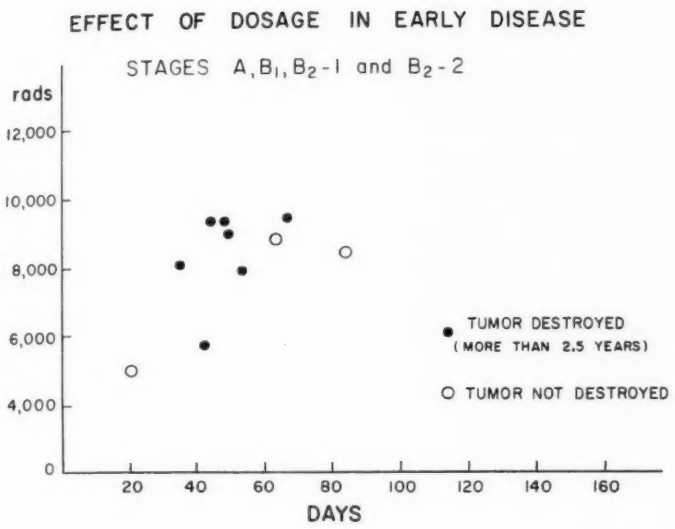

Fig. 10. Doses employed in 11 cases of so-called "early" cancer of the bladder (see Fig. 1).

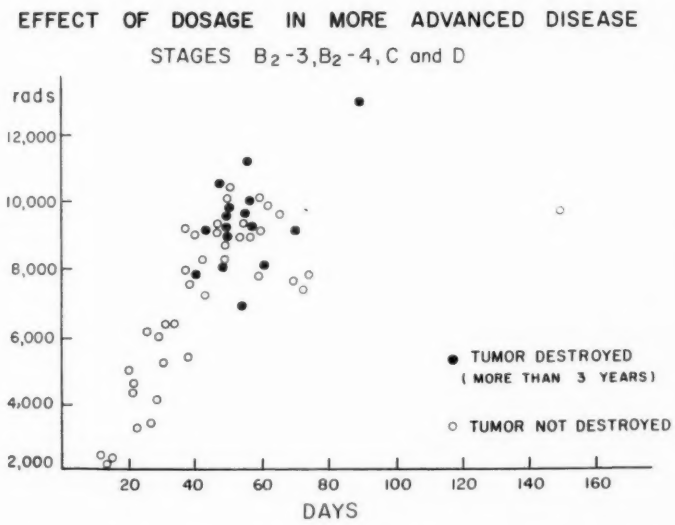

Fig. 11. Tumor doses employed in moderately advanced and advanced carcinoma with metastasis. The "successful" doses are higher than those employed in early cancer. In many cases the tumor was not destroyed with high doses ranging from 8,000 to 10,000 rads. Note the large dose of 13,200 rads in 90 days given to one unusual case described in this paper. Doses lower than 6,500 rads were unsuccessful in this series.

Fig. 12. Demonstration of residual disease in a bladder on the forty-third day of treatment after delivery of a maximum tumor dose of 8,447 rads. Because of this radiographic evidence of residual disease, and because a biopsy showed residual viable-appearing carcinoma, it was decided to increase the total tumor dose to 13,200 r.

centage of tumors or whether rotation technics are preferable with the betatron for bladder cancer.

AN UNUSUAL CASE

One unusual case was an extensive radioresistant lesion which was given a tumor dose of 13,200 rads in ninety days, with production of necrosis of the bowel which was corrected surgically.

I. M., a white female aged 35 years, had hematuria in July 1957. On Aug. 5, 1957, a large lesion on the left lateral bladder wall was coagulated transurethrally. The histologic report was "papillary carcinoma with infiltration, Grade 3." Four days later, because of severe hemorrhage, the bladder was opened and the lesion fulgurated. On three subsequent examinations during the next two months, the recurrent or persistent tumor was fulgurated. On the last examination, Oct. 29, 1957, a large fungating, infiltrating tumor, 4 cm. in diameter, was present on the left lateral wall. In addition, four seedings were seen on the dome and three at the base of the bladder. These were not coagulated. On bimanual abdominovaginal examination, without anesthesia, a 2 × 4-cm. movable mass on the left wall of the bladder was easily palpated.

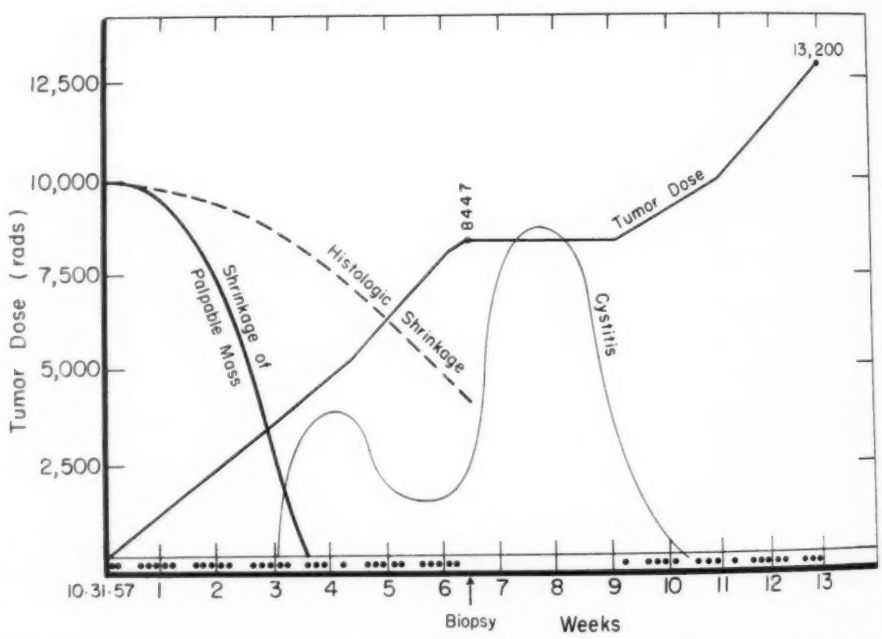

Fig. 13. Graphic representation of treatment and reactions in an unusual case. Each dot along the abscissa represents an x-ray treatment. Note the rapid shrinkage of the palpable mass, which led to an early erroneous opinion that the tumor was radiosensitive. The histologic shrinkage curve was based on the serial biopsy. There was residual disease after a tumor dose of 8,447 rads in forty-three days. The cystitis was intensified by the secondary infection following the interim biopsy. Hence the total dose was raised to 13,200 rads in ninety days. Patient free of disease today (July 31, 1959).

The lesion was classified as "Stage B_2—Grade 3, multiple, recurrent."

Supervoltage rotation irradiation was started on Oct. 31, 1957 (Fig. 13). It will be noted on the portal film (Fig. 2) that portions of intestine dip into the anterior and posterior corners of the upper surface of the cylinder of intense irradiation. The palpable mass responded rapidly to irradiation and apparently disappeared by the twenty-fifth day, when the tumor dose was 4,667 rads. The tumor was thought to be moderately radiosensitive and the dose was carried up to 8,447 rads in forty-five days.

Following this a cystogram (Fig. 12) was obtained and biopsy was performed. The cystogram showed a large residual defect caused by the tumor. The cystoscopically visible part of the tumor had shrunk only about 33 per cent. Histologically there were some infiltrating islands and cords of cancer cells showing only slight nuclear changes and cytoplasmic swelling. A plurality of nuclei showed no apparent radiation changes. It was concluded that there was a radioresistant component which required a much larger tumor lethal dose. The biopsy procedure ignited a severe cystitis, which abated after three weeks. Irradiation was then continued until Jan. 29, 1959, when the total tumor dose was 13,200 rads in ninety days.

After one month of severe cystitis, the frequency of urination subsided to every two or three hours. The only skin reaction was transient epilation of pubic hair.

Beginning in October 1958, one year after the first x-ray treatment, the patient complained of hematuria, rectal bleeding, and severe cramps. The hematuria was shown to be due to hemorrhagic cystitis, which abated. The intestinal signs and symptoms led to exploratory laparotomy on Nov. 8, 1958. Two plaques of necrosis of the entire thickness of the intestinal wall were found in the sigmoid colon and terminal ileum (Fig. 14). These loops were probably fixed to the bladder as a result of adhesions following the original cystotomy and thus received about the same dose as the bladder. The patient is alive today (July 1959) without evidence of cancer.

Comment: Only with a well collimated beam of supervoltage radiation could this type of radical treatment be undertaken for an advanced radioresistant cancer of the bladder.

Fig. 14. Radionecrosis with imminent perforation of the sigmoid (on the right) and the ileum (on the left) caused by tissue doses probably somewhat higher than 10,000 rads in ninety days. Note in the port film of this same patient (Fig. 2) a loop of ileum and a loop of sigmoid within the treatment field. They were probably fixed to the bladder by adhesions following the original cystotomy operation and were continually held within the irradiation field.

TABULATION OF CASES

All cases in this series are schematically tabulated in Figures 15–19 in such fashion that they can be rearranged in several groupings for analysis. Inspection of these figures yields several immediate impressions. In most of our cases, the bladder and tumor were subjected to multiple surgical procedures over a period of several years and finally were referred for supervoltage irradiation when the disease had become terminal.

The following key applies to the figures:

KEY TO FIGURES 15 TO 19

——	Life Line
O	Cystotomy
•	Transurethral Resection
◉	Cystotomy and Fulguration
Φ	Segmental Resection of Bladder
R	Radon Seeds or Radium
X	Total Cystectomy
■	Death
⬡	Supervoltage X-ray Therapy
—\—	Other Surgery (Prostatectomy, etc.)

Figure 15 depicts the early lesions, Stages A and B_1 (Grade 1 and 2). The pre-irradiation surgical treatments were fewer in number and there was less delay in starting supervoltage irradiation than in the case of the advanced lesions of Stages B_2 and C, illustrated in Figure 16. The results also were better. This suggests three deductions. A patient with early

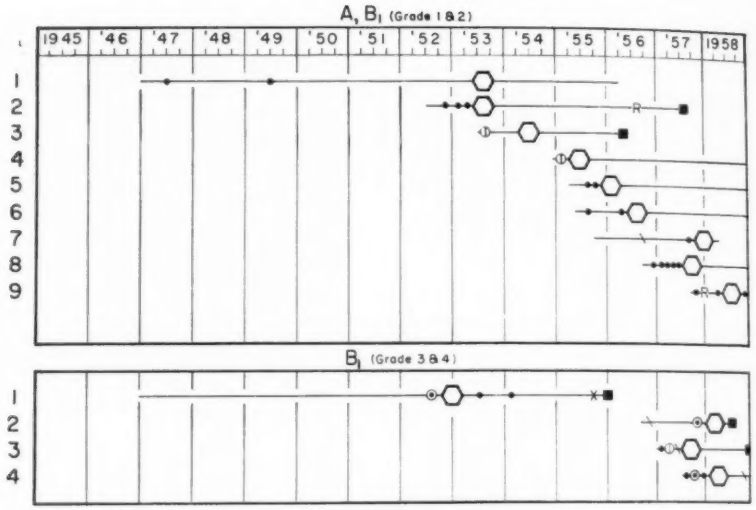

Fig. 15. Diagrammatic representation of the various treatments and progress of patients with early cancer. The subgroup, B_1 (Grades 3 and 4) was independently depicted because of the uncertainty as to whether it should be included in the "early" cases or the "moderately advanced" cases. Note the relative effectiveness of irradiation for "early" lesions. For key to this and Figures 16–19, see p. 201.

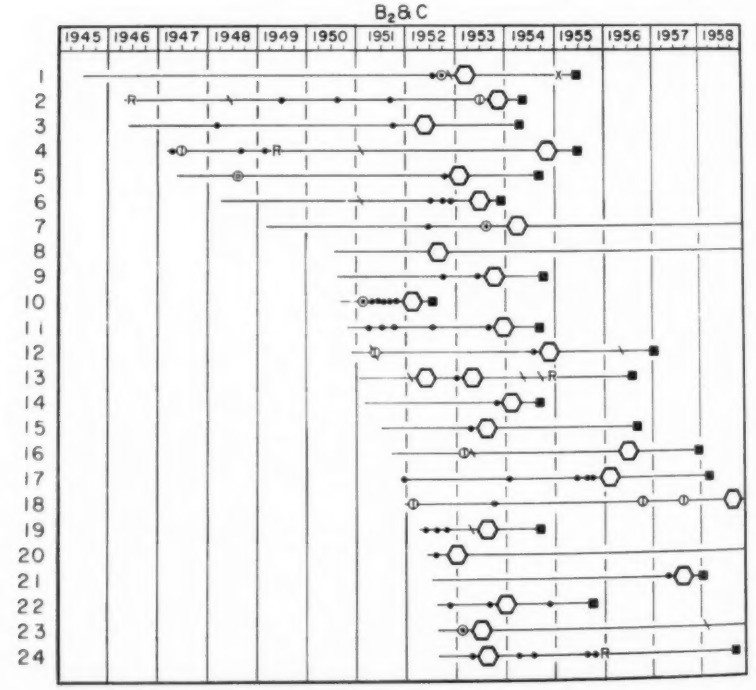

Fig. 16. Diagrammatic illustration of the progress of one-half of the patients with "moderately advanced" cancer, Stages B_2 and C.

papillary carcinoma is bound to have a long survival because of the long life history of this type of tumor. An early cancer responds more favorably to irradiation than an advanced cancer. A bladder not traumatized by multiple surgical procedures can tolerate irradiation better than a scarred bladder.

Comparison of Figures 16 and 17 yields some interesting observations. The charts depict lesions of the same type, *i.e.*, Stages B_2 and C. The patients were aligned according to the time of onset of symptoms. In order to avoid overcrowding, two charts were made. Curiously, the first group of patients (Fig. 16) were subjected to many and different types of surgical procedures; the tumor had a longer life history prior to irradiation; and the average survival time following irradiation was longer than in the second group of patients (Fig. 17), in which the average life history before and after irradiation was shorter. It seems as though the urologist had learned the virtue of starting irradiation early but then referred a more advanced type of lesion for such treatment.

Advanced lesions with metastasis (Stage D) are only occasionally helped by external irradiation (Figs. 18 and 19).

RESULTS

The total survival rates in any series of bladder cancers, such as presented in Table II, is useful as an inventory but not for evaluation of a particular technic, as the results depend on the type of lesions constituting the series. Considering the predominance of advanced lesions, as indicated in Figure 1, the fact that 22 per cent survived three years and 13 per cent survived five years indicates that supervoltage rotation irradiation can play a useful role in the treatment of bladder cancer.

The results, tabulated in a scatter diagram according to Stage and Grade of the

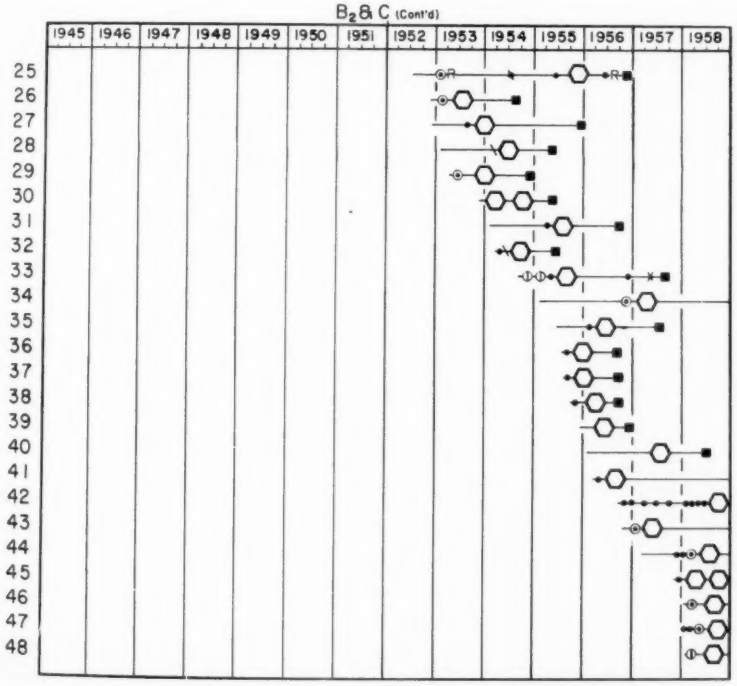

Fig. 17. Diagrammatic illustration of the other half of the patients with "moderately advanced" cancer, Stages B_2 and C.

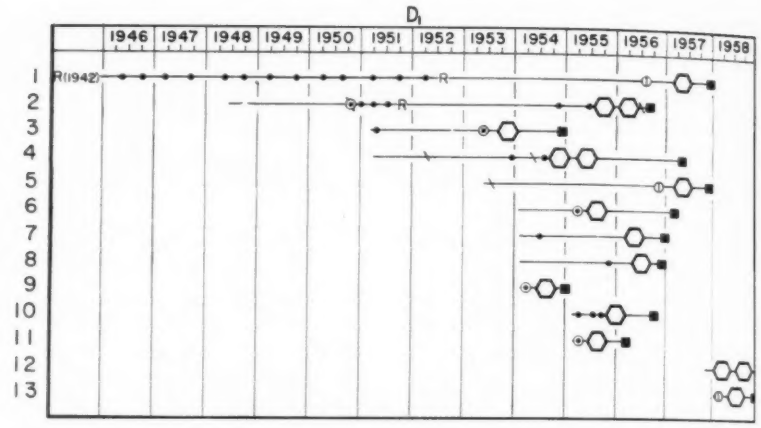

Fig. 18. Diagrammatic illustration of the "advanced" cancers of the bladder with metastasis, Stage D_1.

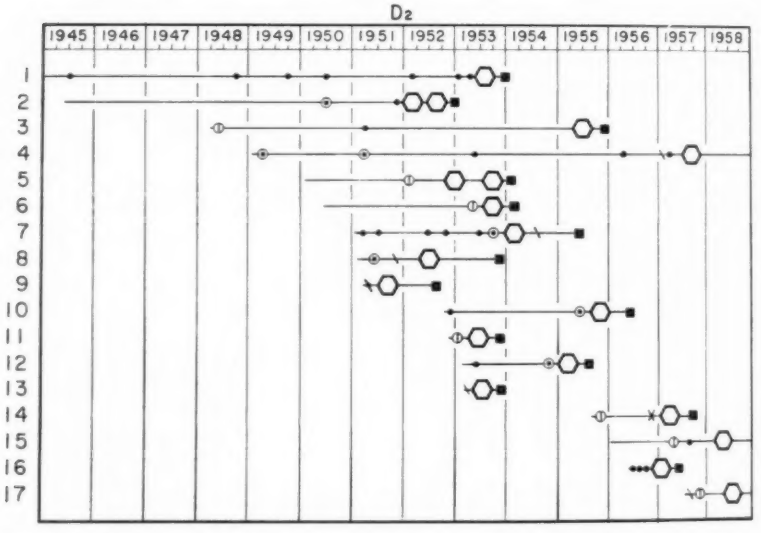

Fig. 19. Diagrammatic representation of the "very advanced" lesions with remote metastasis, Stage D_2.

lesion (Fig. 20), yielded a number of tentative deductions. Treatment is more effective for early than for advanced lesions with respect to stage and grade. Thirteen patients are alive more than three years. Five patients are alive more than five years, and 3 of these had Stage C disease. Generally patients with Stage C and D lesions die in less than two years. Yet 5 patients in this category did not die until the third year. Therefore patients with advanced cancer should not be denied the opportunity for palliative prolongation of life.

Prognosis of Primary vs. Recurrent Cancer: In this series 25 per cent of the tumors were primary and 75 per cent were recurrent. Most of the latter had been treated by various types of surgery, and a few by irradiation. Using three-year survival as

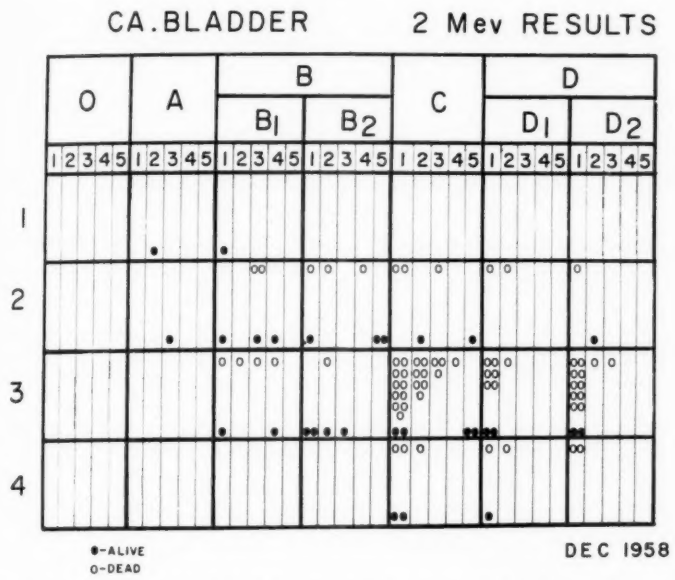

Fig. 20. Results for a period of five years in 81 cases tabulated according to Stage and Grade. The survivals, from one to five years, are indicated in each category. In the "early" cases the prognosis is more favorable than in the "advanced" cases. Note the 3 five-year survivals in Stage C. Life is frequently prolonged for three to four years in Stage C lesions. In Stage D most patients die within one year after institution of irradiation. Nevertheless, an occasional patient lives into the second year.

a parameter, the survival rate for primary tumors was 42 per cent and for recurrent tumors 18 per cent.

The obvious conclusion, that primary tumors respond better to irradiation than recurrent tumors, must be somewhat modified, since the primary tumor represents an earlier phase of the disease and its natural life history would be longer than that of a recurrent tumor. A more accurate deduction would be that, if irradiation is to be employed, it should be instituted early in the course of the disease.

Comment on Results: In order to assay the role of supervoltage rotation irradiation, or for that matter in order to evaluate

TABLE II: CARCINOMA OF THE BLADDER. RESULTS OF 2-MEV THERAPY

	Number of New Cases	Survivors, One to Seven Years						
		1	2	3	4	5	6	7
1951	2	0	0	0	0	0	0	0
1952	7	6	5	3	2	2	1	..
1953	22	18	10	6	2	2	..	..
1954	9	7	3	1	1	..	..	..
1955	18	14	7	4	..	..	..	..
1956	9	4	2	..	..	..	..	..
1957	14	9	..	..	..	..	..	..
Summary of Results								
Years after Treatment →		1	2	3	4	5	6	7
No. treated		81	67	58	40	31	9	2
No. alive		59	27	13	5	4	1	0
Per cent alive		73	40	22	13	13	11	0

TABLE III: PROGNOSIS OF PRIMARY *vs.* RECURRENT CANCERS

(3-Year Survivals)

At risk	45 cases
Primary	25%
Recurrent	75%
Primary tumors (5 of 12 survived)	42%
Recurrent tumors (6 of 33 survived)	18%

any of the new surgical and irradiation technics for cancer of the bladder, much more extensive clinical study will be required than this type of preliminary pilot study. A co-operative clinical study by a number of clinics, with randomization of cases could provide relatively early answers and possibly save lives.

The greatest cause of failure is the delay due to prolonged use of repeated transurethral fulgurations in the early phases of aggressive cancers. In this series, 75 per cent of the cases had had previous treatment, mostly surgical.

REACTIONS

Irradiation cystitis, a major obstacle in radiotherapy of bladder cancer, is much more severe with external irradiation than with central source intracavitary irradiation. The cystitis is intensified in the presence of post-surgical and post-coagulation scarring and by diffuse carcinomatous infiltration of the bladder wall.

In many instances of advanced cancer, the irradiation palliation is neutralized by the intense discomfort of the associated cystitis. One is prompted not to irradiate Stage D lesions, but the occasional prolongation of life for more than a year (Figs. 18 and 19) prompts consideration of palliative irradiation for advanced cancer. For example, in Stage D_1 cases, 3 of 13 patients survived for more than one year; and in Stage D_2 cases, 3 of 17 patients survived for more than one year.

COMPARISON OF TECHNICS

Three technics are compared in Table IV: radical surgery (4), supervoltage rotation, and a central intracavitary source (2). The number of cases in each category is too small for solid conclusions, but some tentative deductions may be made.

Of the two irradiation technics, the central intracavitary source yielded far better results than supervoltage rotation irradiation.

Irradiation achieved no three-year or five-year arrests in Stage D cases, whereas surgery arrested an occasional lesion with node metastasis. It is probable, however, that some Stage C lesions arrested by irradiation actually may have had node metastases which were not demonstrable clinically.

When supervoltage rotation therapy is compared with radical surgery, the three-year results favored irradiation slightly. There were no irradiation cases at risk more than five years. Surgery was used on more favorable cases, *i.e.*, 30 per cent of the surgical cases were in the early Stages, 0, A and B_1 categories, whereas supervoltage irradiation was used in only 8 per cent of the early cases. In the intermediate group, Stages B_2 and C, supervoltage irradiation was used more often than surgery, *i.e.*, 48 as compared with 38 per cent of the cases, and achieved somewhat better three-year and five-year arrests.

In comparing the total figures of super-

TABLE IV: BLADDER CANCER: COMPARISON OF TECHNICS

Stage	Whitmore: Cystectomy (160 cases)			Friedman: 2 Mev Rotation (81 cases)			Friedman and Lewis: Central Intracavitary Source (50 cases)		
	% Cases	% 3-yr. Survival	% 5-yr. Survival	% Cases	% 3-yr. Survival	% 5-yr. Survival	% Cases	% 3-yr. Survival	% 5-yr. Survival
0, A, B_1	30	55	44	8	62	..	37	93	85
B_2, C	38	16	9	48	27	16	53	48	47
D	32	6	4	45	0	0	10	0	0
TOTALS	100	25	18	100	22	13	100	54	56

voltage irradiation with surgery, the latter figures were found to be slightly but not significantly higher. Surgery was employed, however, in a higher percentage of early cases. In any event, the irradiation results with the central intracavitary source were superior to those with either of the other two technics.

CONCLUSIONS

1. In a series of 81 bladder cancers most of which were extensive and advanced, irradiation with two-million-volt x-rays by the rotation technic achieved a 22 per cent three-year arrest rate and 13 per cent five-year arrest rate.

2. The successful doses ranged from 8,000 to 10,000 rads in forty to sixty days. An occasional case required larger doses. These doses are higher than reported by others (11, 12, 13). They were dictated by the findings at serial cystoscopic examination, with biopsy, during treatment, and by the frequent finding of residual disease after doses as high as 7,000 and 8,000 rads. We cannot as yet reconcile our large doses with the smaller dosage reported by others, but believe that advanced highly malignant bladder cancers require large tumor doses. These large doses can be given only with a well collimated beam of supervoltage x-rays or gamma rays, with a precision beam-aiming technic.

3. In order to improve the results of irradiation of bladder cancer, the prevalent practice of multiple surgical procedures prior to irradiation will have to be discontinued, and irradiation started when the disease is in an earlier phase.

4. Radiation cystitis is more severe following supervoltage rotation irradiation than following the central source intracavitary technic.

5. The irradiation results in the treatment of primary tumors are higher than for recurrent tumors, 42 per cent *vs.* 18 per cent three-year survivals.

6. An unusual case is described, wherein a highly malignant, Stage C, radioresistant carcinoma was radically irradiated with a maximum tumor dose of 13,200 rads in ninety days and the disease controlled. Injury to the intestines was corrected surgically.

7. In my own experience the central intracavitary source (Walter Reed technic) is superior to supervoltage rotation irradiation for bladder cancer. It yielded a 56 per cent five-year apparent arrest rate compared with 13 per cent five-year survival rate.

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SUMMARIO IN INTERLINGUA

Irradiation Rotational a Supervoltage (2 Mvp) in Cancere del Vesica

In un serie de 81 casos de cancere del vesica—generalmente extense e avantiate—irradiation per radios X de 2 milliones volt secundo le technica de rotation resultava in 22 pro cento de arrestos trienne e 13 pro cento de arrestos quinquenne.

Le doses effectuante iste successos variava inter 8.000 e 10.000 rads in quaranta a sexanta dies. In certe casos, plus grande doses esseva requirite. Iste doses es plus grande que le doses reportate per alteres. Illos esseva dictate per le constatationes facite in examines cystoscopic serial—con biopsia—durante le tractamento e per le frequente observation de morbo residue post le application de doses attingente 7.000 e 8.000 rads. Doses de un tal magnitude pote esser applicate solmente con un ben collimate fasce de radios X de supervoltage o de radios gamma con un technica de precise visation de fasce.

Pro meliorar le resultatos del irradiation de cancere del vesica, le nunc prevalente practica de multiple operationes chirurgic ante le irradiation debe esser abandonate e le irradiation debe esser initiate quando le morbo es ancora in su stadios precoce.

Le resultatos de irradiation es plus favorabile in le tractamento de tumores primari que in le casos de tumor recurrente. Le superviventias trienne in iste duo situationes es 42 e 18 pro cento, respectivemente.

Es describite un caso inusual in que un malignissime carcinoma radioresistente del stadio C esseva irradiate radicalmente con un dose maximal al tumor de 13.200 rads in novanta dies. Stabilisation del morbo esseva effectuate. Injurias al intestinos esseva corrigite chirurgicamente.

In le experientia personal del autor le uso de un fonte intracavitari central (technica Walter Reed) se ha provate superior al irradiation rotational a supervoltage in le tractamento de cancere del vesica. Illo resultava in apparente arresto quinquenne in 56 pro cento del casos, durante que le presente serie monstra un superviventia quinquenne de 13 pro cento. Es etiam a signalar que cystitis de radiation es minus sever in le technica a fonte intracavitari central.

Supervoltage Irradiation in Bladder Carcinoma: 1952–1958[1]

PHILIP RUBIN, M.D., and ROBERT BURAN, M.D.[2]

CARCINOMA OF THE bladder represents a spectrum of disease ranging from benign papillary carcinoma to a highly invasive and aggressive anaplastic tumor. The variability of its course and lack of a generally acceptable classification has obscured rather than clarified the problem. This is not to imply that a dearth of literature exists on this subject, but the absence of a generally accepted clinical grading which can be utilized by both the urologic surgeon and radiotherapist is reflected by the variety of systems proposed.

Patterson suggests the division of bladder carcinoma simply into noninfiltrating and infiltrating varieties. In contrast, Friedman (7) has designated twelve clinicopathologic types for convenience and suggests that twice this number actually exist and would aid in determining treatment and predicting prognosis. This leads to a dilution of numbers and makes it difficult to report results. A pure clinical grouping, as suggested by Rusche and Jaffe (13) fails to consider the histology, which is as important in classification as anatomical extent.

Recently, accurate classification systems have been evolved by leading urologists. These systems are reduced to two essentials known to influence prognosis: (*a*) the physical extent or depth of infiltration of the tumor; (*b*) its inherent aggressiveness or histologic grade. Accordingly, Marshall's dual classification (12), which permits evaluation of a given tumor as to its inherent vigor (grade) and present anatomic extent (stage) seems most worthwhile. This is, however, a surgical and not a clinical classification, which in many instances does not allow for grouping of all patients treated by radiation therapy.

Marshall (12) states that "no one knows what proportion of vesical cancers fall into what stage at the time the patients present themselves for treatment." This is borne out by the fact that 40 per cent of his patients with deeply invasive lesions (B2 and C groups) had histologically positive nodes at a time when routine preoperative studies did not indicate such carcinomatosis, implying stage D lesions. He rightly concludes that specimens removed by radical cystectomy or pelvic extenteration should provide firm knowledge in this respect. Such a "biopsy procedure" for accurate classification, however, eliminates the need for additional therapy.

In attempting to evolve a meaningful classification, the factors to be regarded can be divided into *primary* or essential considerations as to the prognosis or evolution of the disease in an average patient and *secondary* factors or considerations as to the success of treatment in a specific individual. That is, a slow growing, superficial carcinoma, classified according to primary factors, should show a favorable response to a simple form of therapy, but may terminate fatally in the presence of an associated advanced cardiac disease.

CLASSIFICATION

A. Primary Considerations

1. *Anatomic Factors:* (*a*) *Depth of penetration* into the wall and perivesical tissue is the single most vital factor determining the outcome of carcinoma of the bladder. Jewett's studies (9) in 107 autopsied cases established a correlation between the degree of infiltration into the bladder wall and the incidence of regional and distant metastases. Potential curability, which is inversely related to metastatic spread, is listed as 100 per cent for submucosal involvement, 89 per cent for muscular, and 26 per cent for perivesical invasion.

[1] From the Division of Radiotherapy, Department of Radiology, Strong Memorial Hospital, Rochester, N. Y. Presented at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

[2] Trainee, National Cancer Institute.

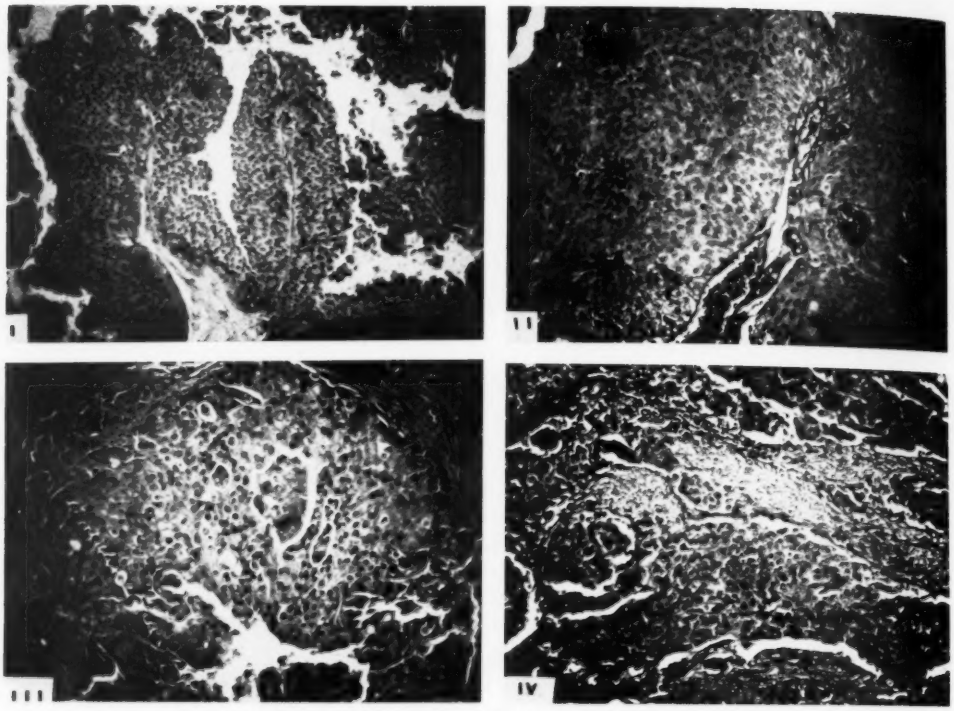

Fig. 1. Histologic grades of bladder tumors: I, II, III, IV.

(*b*) *Surface area* or circumferential spread has also been correlated with the depth of invasion of the tumor and ultimate prognosis, by Baker (1). Limited vesical spread is associated with superficial extension to the submucosa and muscle, whereas tumor cells may spread through 60 per cent of the bladder circumference with deep muscular invasion and be associated with 80 per cent positive nodes.

(*c*) *The solitary or multiple nature* of polypoid tumors is an important consideration in therapy, though of less significance as to outcome. A large mass arising from a small stalk is a more favorable lesion than a conglomerate mass of polyps arising on a broad base. The thickness of the lesion varies considerably and is of less prognostic importance as the exophytic component exceeds the endophytic extent.

(*d*) *Location of the lesion* is meaningful in respect to metastatic spread in that the lymphatics of the posterior wall and base of the bladder run a longer course before leaving the bladder than those which drain the lateral walls. The trigone of the bladder is less expansile, its muscular zone is not as active or contractile as the walls and fundus. Thus, one series showed double the number of metastases from lateral wall lesions as compared to disease of the posterior wall (10). On the other hand, tumors of the trigone may involve the ureteral orifices and carry a higher complication rate than lesions on the dome. Bilateral metastases probably will occur more frequently with anterior wall lesions, as the vesical and perivesical lymphatics cross over this zone (2).

2. *Histologic Factors:* The generally accepted grading of bladder tumors depends on the degree of alteration in normal architecture, loss of polarity of cells, number of mitoses, etc. Four grades, I to IV, are utilized by most pathologists (Fig. 1).

Grade I: Regular funnel-like papillary masses separated by evenly spaced connective-tissue septa. Individual

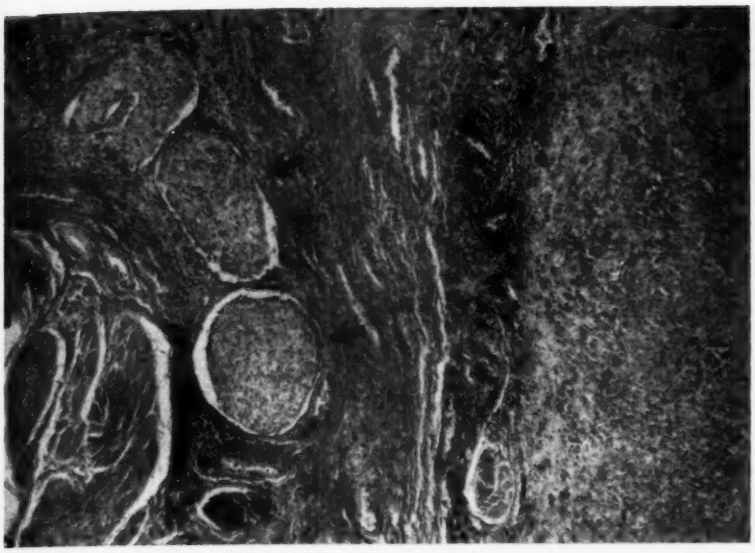

Fig. 2. Invasion of lymphatics and vessels can be determined only on deep biopsy, since circumferential spread generally occurs in the muscularis.

cells are uniform in appearance with abundant cytoplasm.

Grade II: The papillary nature persists but the connective-tissue septa are irregularly spaced, often embracing relatively large masses of cells. In focal areas, mitotic activity is high and some nuclei have little cytoplasm.

Grade III: Patchy distribution to papillary tumors and cell masses appear to be breaking up into smaller groups. Mitoses are frequent.

Grade IV: Papillary areas are rare and appear as small nests of cells with deep-staining small nuclei. Mitoses are very frequent and atypical, with little cytoplasm in cells.

Grade V: Unusual tumors which are either metaplastic squamous-cell carcinomas or adenocarcinomas.

Invasion of muscle, lymphatics, and vessels can be determined on adequate deep specimens (Fig. 2).

3. *Diagnostic Studies:* The diagnostic work-up to determine these primary factors should include the following:

(*a*) *Bimanual examination under spinal anesthesia*, when correlated with microscopic findings, should segregate noninfiltrating from infiltrating tumors. Jewett (8) has stressed the importance of this approach and has outlined the four stages in the progress of the infiltration commonly encountered clinically and the three common sources of error in the interpretation of palpable induration. Generally, one can distinguish infiltration limited to the bladder wall from extension into the perivesical tissues, but in many instances biopsy is vital for determination of the degree of invasion within the wall. Commonly associated inflammation may lead to overstaging which is difficult to evaluate. On the other side of the coin, positive nodes, as mentioned by Marshall, are not recognized in deeply invasive cases, leading to understaging in a significant group of patients.

(*b*) *Cystoscopic study* in association with an experienced urologist is essential to determine such factors as thickness, location, and multiplicity of lesions, as well as the general state of the mucosa. The concept of ability to palpate cancer cell dissemination is nearly as untenable as determination of the peripheral or infiltrative spread visually, according to Baker. For this the next step is necessary.

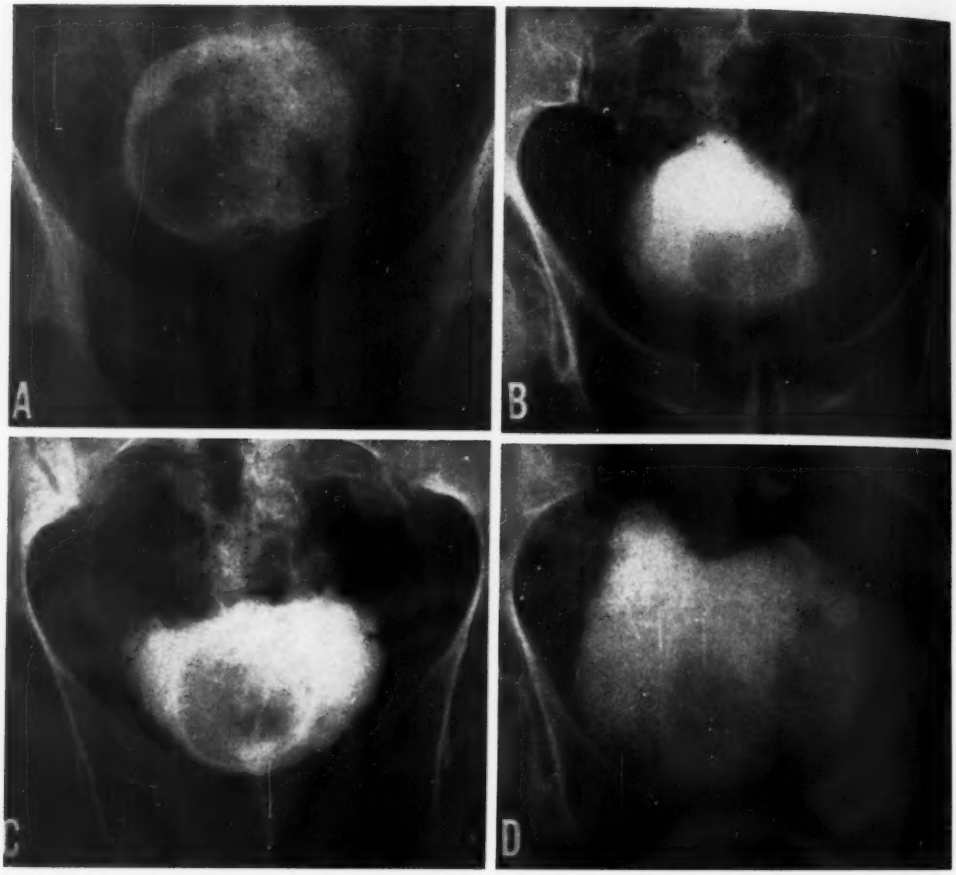

Fig. 3. Cystograms are rarely of value in determining the degree of infiltration and fixation. Selection by stage corresponding to A, B, C, D depths in Marshall's classification shows that filling defects vary in size independent of the stage of invasion. (Letter and stage correspond.)

(*c*) *The biopsy specimen* should be representative of the lesion to be treated. *Multiple specimens* should be obtained from large solitary lesions, or samplings of various polypoid areas if the lesions are many in number. When several biopsy specimens are studied, it is not unusual to find various grades of neoplasia present in one patient. The ultimate outcome is obviously dependent on the most advanced grade. Superficial biopsies yield only superficial knowledge. If possible, the specimen should be deep enough to include the muscularis, so that degree of penetration can be determined, and some information obtained as to the state of vascular and lymphatic invasion. Ideally, biopsies should be taken from the growing edge rather than the center of tumors and include some normal tissue for a landmark.

(*d*) *Radiographic studies*, as cystograms, are rarely of value in determining the degree of infiltration and fixation (Fig. 3). Filling defects vary in size, independent of the stage of invasion, and reflect the exophytic rather than the endophytic component. In routine studies, masses are occasionally obscured by the excess of radiopaque material injected into the bladder but can be visualized on contrast-air studies. The capacity of the bladder can be determined at cystography and is a

Fig. 4. Cystograms and pyelograms yield different bits of information: A cystogram (A) is best for determining bladder capacity. A pyelogram (B) records the status of the kidney and ureters in the same patient.

useful follow-up parameter. Bladder filling on pyelography should never be substituted for cystography as a measure of bladder volume (Fig. 4).

Intravenous pyelograms are of value in determining the status of the ureters. Associated hydronephrosis in and of itself does not signify an advanced stage in every instance but generally is a complicating factor and may be a poor prognostic sign. Relief of hydronephrosis or its induction may occur following a course of radiotherapy, suggesting the need for follow-up pyelograms (Fig. 10).

CLASSIFICATION

B. Secondary Considerations

1. *General state of health* is an important secondary consideration. The relatively advanced age of this group of patients is readily apparent. Our series is composed mainly of persons sixty to eighty years of age, and associated geriatric diseases, as arteriosclerotic heart disease, hypertension, heart failure, chronic pulmonary lesions, and even other malignant tumors were not uncommon.

2. *Associated urologic complications* demand careful management and often determine whether therapy will be successfully tolerated and completed as proposed. *Prostatism* is not uncommon, requiring transurethral resection to allow for adequate drainage prior to radiation therapy to avoid problems of retention and associated infection. *Control of bacterial infection* is vital if severe cystitis and ascending pyelonephritis are to be averted. *Ureteral obstruction* must be corrected if loss of kidney function is to be prevented, with the attendant uremia. *Anemia due to hematuria* not only makes transfusions necessary from a general care point of view, but radiobiologic evidence suggests that the responsiveness of tumors to irradiation can be lowered in the anemic state. Hemoglobin levels of 12 gm. and hematocrits of 30 per cent should be maintained.

3. *Recurrent lesions* are generally more aggressive and refractory than primary

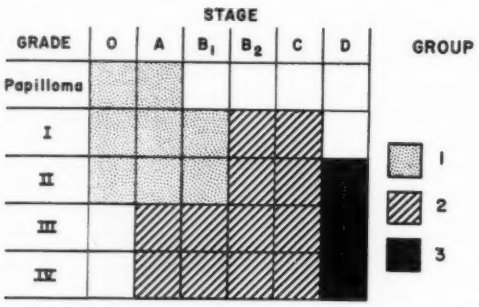

Fig. 5A. Proposed clinical classification superimposed on Marshall's surgical classification.

tumors and have a poorer prognosis. Friedman (7) showed that the three-year survivals dropped from 65 per cent for primary lesions to 48 per cent for recurrences.

4. *Previous surgery* has very frequently been performed in patients with bladder tumors presenting for radiation therapy. Fulguration is not vital to the outcome of future radiation therapy unless it is deep, down to the serosal coat. This thinning of the bladder wall may lead to perforation if the tumor recurs at this site. Likewise, segmental resection adds to the risk of perforation and fistulas if the tumor proliferates at the site of resection and is later destroyed by radiation therapy.

5. *Previous radiation therapy* adds to the risk of supervoltage therapy and lowers the chances of a successful outcome. Isotopes instilled into balloons or directly into the bladder for superficial lesions probably are less significant in this respect than radium and interstitial radon or radioactive material. Sources which are not removed may act as secondary irradiators and lead to localized ulceration.

PROPOSED STAGING

The series herein presented is analyzed along the lines of a modified dual classification as outlined by Marshall (12), Jewett (9), Cuccia (6), and others, in which both anatomic extent of penetration and histologic grade are considered as the major items (Fig. 5A). A clinico-pathologic classification is feasible, since there is a proportionate relationship between stage and grade. As in other series (7, 11) most cases fall on a diagonal from upper left to lower right, while those eccentrically classified might be expected to behave differently. With this approach, three general groups exist (Fig. 5B):

Group 1:	Superficial Stage (0, A, B_1)	Low Grade (I, II)
Group 2:	Deep Stage (B_2, C)	High Grade (III, IV, V)
Group 3:	Metastatic Stage (D)	High Grade (III, IV, V)

In Group I are those papillomas that show some evidence of invasion and atypical features histologically. These lesions are slow growing and of low-grade malignancy.

Included in Group 2 are those cases *either* with deep anatomic invasion or of an advanced histologic grade. Admittedly, patients in whom only one of these factors is present, rather than both, have a better prognosis and may render the survival figures of this group better than they really are. Nevertheless, the limitations of the diagnostic methods do not allow for sufficient accuracy of staging. It would seem wisest to include all tumors with evidence of biologic aggression by virtue of *either* deep stage or high grade in this group, and the philosophy of treatment is the same.

Once definite extension of the infiltrative process is noted in the surrounding perivesical tissues up to the pelvic wall by bimanual palpation, the case is staged as metastatic. Probably this represents a more advanced group than the surgical metastatic D, since isolated nodal metastases are not as early recognizable by digital examination.

The reasons for employing supervoltage irradiation in each group will be outlined and the results to date will be presented, following an outline of the technic of treatment and the dosages delivered within certain time limits.

BLADDER CARCINOMA AT STRONG MEMORIAL HOSPITAL: 1952–1958

Our total group of bladder carcinomas consists of 78 cases, of which 61 were

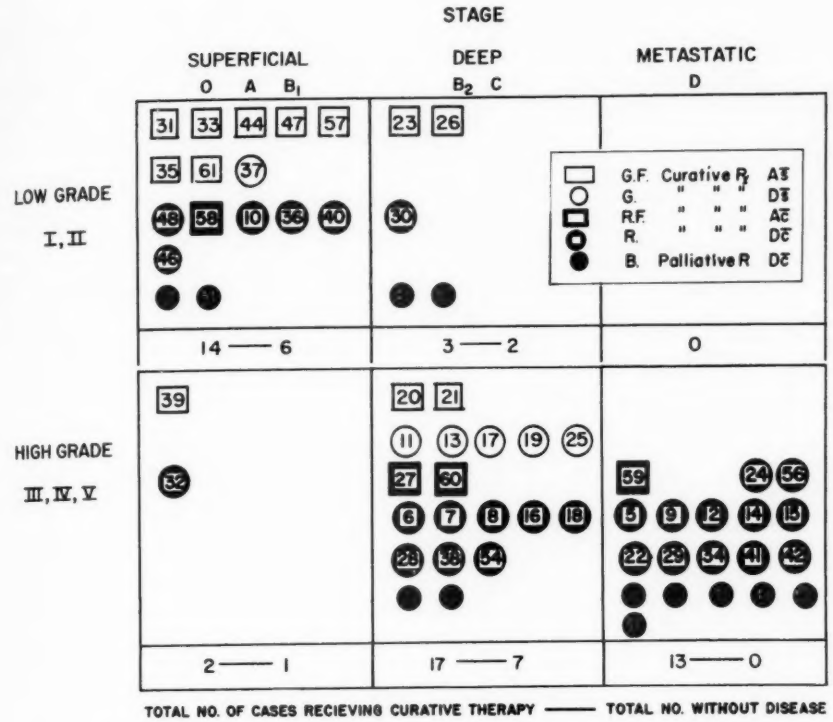

Fig. 5B. Distribution of cases in modified clinicopathologic classification.

treated by 1-Mv rotational supervoltage irradiation and constitute the present series. By way of general information, the sex incidence in this series was predominantly male (83 per cent) and the majority of the patients were between sixty and eighty years of age (67 per cent). The commonest presenting symptoms were hematuria (57 per cent), frequency (51 per cent), and dysuria (38 per cent). Nocturia occurred in 16 per cent, and pain in 15 per cent. Suprapubic and deep pelvic pain is an ominous symptom. On cystoscopic examination, 63 per cent of the patients had multiple lesions as opposed to solitary papillary lesions. The most frequent anatomic sites of origin were the trigone (33 per cent) and bladder neck (33 per cent) followed by the lateral walls (21 per cent) and diffuse involvement (16 per cent). The fundus was involved in 5 per cent, the posterior wall in 7 per cent, and the anterior wall in 5 per cent. It is interesting to note that this distribution differs from that reported by the Carcinoma Registry of the American Urologic Society, where 42 per cent of the carcinomas arose on the lateral walls, 27 per cent on the trigone, and 6 per cent in the bladder neck.

TECHNIC OF 1-MV SUPERVOLTAGE ROTATIONAL IRRADIATION

Once the diagnostic work-up is completed, a Foley catheter is inserted prior to therapy and mercury is injected into the balloon and air into the urinary bladder. Localizing films at right angles are taken in an erect position with the patient resting on a bicycle seat. Either 270° oscillation or 360° rotational therapy is begun depending upon the size of the patient and location of the tumor. The axis of rotation is located along the posterior wall of the bladder rather than in the center of the tumor. Since the

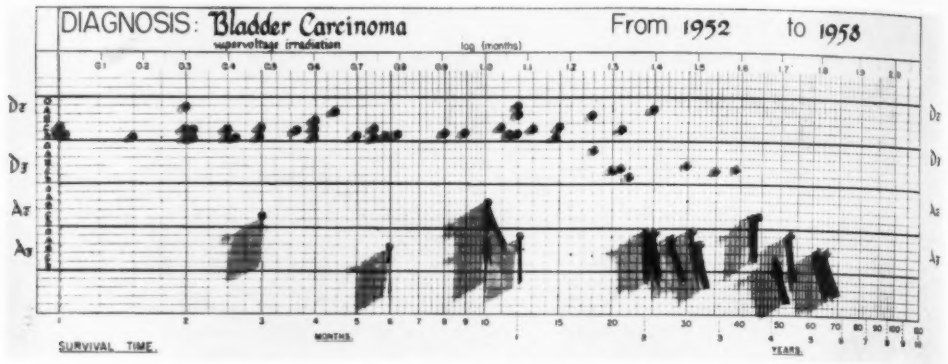

Fig. 6. Boag follow-up system as applied to bladder carcinoma.

axis of rotation is eccentric to the geometric axis of the patient, the isodose curves are shifted anteriorly. By leaving out the posterior 90° in oscillation, the dose to the rectum is lowered and proctitis is avoided. Repeat localizing films are taken at one- or two-week intervals during treatment. If the patient is unable to co-operate, he is treated through three oblique fixed fields, with cross-firing of the bladder as outlined by Buschke *et al.* (4).

The daily tumor dose generally was 200 r at the axis of rotation, with a variation of ± 10 per cent throughout the tumor and bladder area. The total tumor dose ranged from 5,000 to 6,000 r in five or six weeks, with doses of 3,000 to 4,000 r reserved for palliative rather than curative purposes. In more recent years, the tumor dose of 6,000 r has been considered the minimal tumoricidal dose required and is delivered in six weeks. The field size usually ranged from 8 × 8 to 10 × 10 cm. If extensive pelvic disease existed, larger fields, up to 15 × 15 cm., were employed.

FOLLOW-UP SYSTEM

Essential to any evaluation is a meticulous follow-up system. All cases at Strong Memorial Hospital are cross-indexed by disease in the departmental files and the tumor registry. All of the 61 cases treated by 1-Mv supervoltage irradiation have been traced since such treatment was initiated in 1952. Cystoscopy is performed at the end of treatment, with repeat examinations scheduled every two to four months during the first year and at lengthening intervals as the disease appears to be controlled.

A modified Boag system (3) of following the patients is utilized, with the plotting of cases on semilog graphs with the use of map-pins and flags of various colors (Fig. 6). A key is worked out according to the problems in each field and is usually arranged in four categories:

Dead, with disease	red pin
Dead, without disease	green pin
Alive, with disease	red flag
Alive, without disease	green flag

The dead patients are shown as fixed pins and the live patients are flagged with name, hospital number, and stage of disease. As the patient is seen in the follow-up clinic, the flag is advanced, so that a current picture is always available. Recurrences must be histologically proved if possible, or at least established by cystoscopy.

RESULTS IN GROUP 1

Superficial Stage (*0, A, B*$_1$) *Low Grade* (*I, II*)

In this early phase of bladder carcinoma, the survival of the patient is quite independent of the disease, in that its presence rarely causes his death (Table I). Upon further analysis of the 57 per cent without disease it is seen that in virtually all patients, if followed long

enough, new lesions or recurrences develop. Thus, 6 of the patients required additional surgery following a course of supervoltage irradiation. Two of the recurrent lesions, due to their multiplicity and associated cystitis, required cystectomy. Fulguration of small new excrescences was accomplished in 4 cases on routine follow-up cystoscopies without evidence of resurgence of the original lesions. It is of interest that Buschke (4) and

TABLE I: BLADDER CARCINOMA: LOW-GRADE (I, II), SUPERFICIAL STAGE (0, A, B_1)

Total Number	16 cases
Curative Therapy	14 cases

	Without Disease	With Disease
Alive	7	1
Dead	1	5
TOTAL	8	6

Total Without Disease	8 cases (57%)
No further therapy	2
Subsequent radiation	0
Subsequent surgery	6
For new lesions	4 (fulguration)
For recurrence	2 (cystectomy)
Conclusion	
6 cases controlled by irradiation (44%)	
5 survivals without disease (35%)	
Survival in Years	
Alive without	4.3, 2.5, 2, 2, 1, 0.8, 0.6
Dead without	1.5
Cause of Death in	8 cases
Persistent carcinoma	7 cases
Uremia	2
Metastases	2
Cardiac	3
Without carcinoma (Uremia)	1 case

Cuccia (6) reported similar frequent recurrences following irradiation for low-grade superficial carcinomas.

All therapeutic attempts to arrest the disease should be conservative initially. The demise of the patient (see Table I) may be due to vigorous therapy rather than an alteration of the carcinoma to a more malignant biologic course. Two of the deaths from uremia followed ureteral transplantation, though location of the papillomatous lesions may well have resulted in obstruction eventually. In only 2 cases in this group was the growth potential altered following irradiation, with development of extensive distant metas-

TABLE II: BLADDER CARCINOMA: HIGH-GRADE (III, IV, V), DEEP-STAGE (B_2, C)

Total Number	26 cases
Curative Therapy	22 cases

	Without Disease	With Disease
Alive	5	2
Dead	5	10
TOTAL	10	12

Total Without Disease	10 Cases (45%)
No further therapy	9
Subsequent radiation	1
Subsequent surgery	0
Conclusion:	
10 cases controlled by irradiation (45%)	
5 survivals without disease (23%)	
Survival in Years	
Alive without	5, 5, 4, 2.5, 2.3
Dead without	3.4, 3, 1.8, 1.8, 1.7
Cause of Death in	18 cases
Persistent carcinoma	13 cases
Uremia	8
Metastases	2
Cardiac	2
Pneumonia	1
Without carcinoma	5 cases
Uremia	1
Hemorrhage	1
Cardiac	3

tases to abdominal viscera and lungs. That cardiac deaths were common reflects the frequency of associated geriatric diseases in this group.

From a study of the plotted course of these cases (Fig. 7), it would appear that most forms of therapy are capable of arresting the disease, but few measures short of cystectomy can cure it. In actuality, such simple surgical measures as fulguration, transuretheral resection, and segmental resection prove adequate and there is little need for radiotherapy. As the disease recurs more frequently, becomes multiple in origin, and changes in its histologic grade and depth of invasion, more radical measures are justified. From the radiotherapeutic point of view, isotopic instillations in a balloon should take care of the earlier superficial lesions limited to a few millimeters, while radium or cobalt interstitially or as a central source may control lesions of greater thickness up to 1 cm (5). Supervoltage irradiation is employed when the only alternative is total cystectomy. It should not be used as a prophylactic measure.

In more instances than not, some form

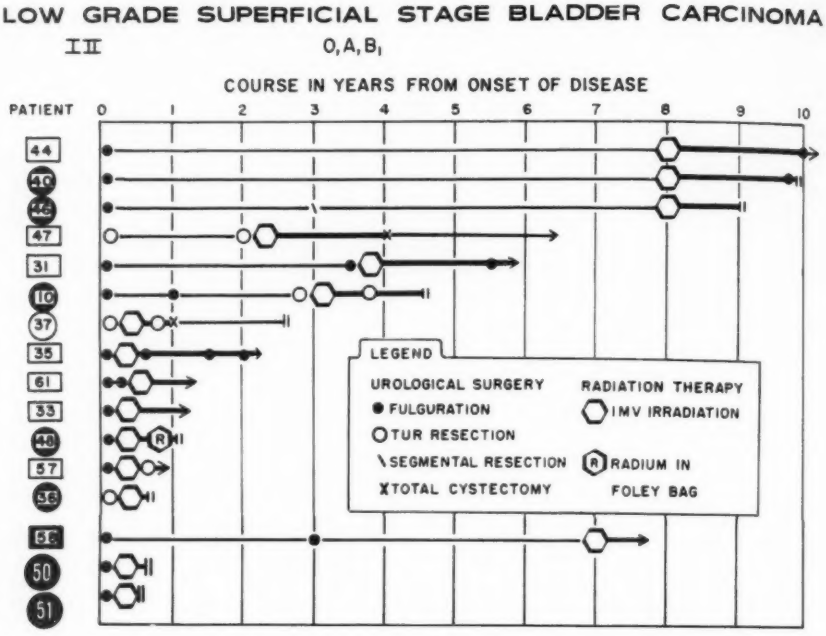

Fig. 7. Plot of cases in Group I indicating the long course patients may have. This appears to be independent of the type of treatment.

of simple surgical therapy was attempted first and 1-Mv irradiation was utilized when this proved inadequate. For this reason, comparison with surgical series in this stage is uninformative, as the latter represent more favorable cases. It is curious that a summary review of five-year results in this particular group shows poorer results with more radical surgical methods (9). This suggests case selection rather than that the more radical methods have less to offer in terms of cure. Another possible explanation is that more radical methods involve ureteral transplantation, with higher mortality.

RESULTS IN GROUP 2

Deep Stage *High Grade*
(B_2, C) *(III, IV, V)*

Group 2 represents the real challenge in bladder carcinoma. The aggressiveness and invasiveness of the tumors is established; if left untreated, they will invariably lead to death as opposed to the previous group. Of the 22 cases which received a full course of therapy, 45 per cent have been controlled by irradiation only (Table II). In 1 instance, recurrence was controlled by further radiotherapy—radium in a Foley bag—although in 2 others a repeat course of 1-Mv irradiation was unsuccessful. Most of the survival figures show the patients to be beyond two years from the date of irradiation, not from the appearance of symptoms. For bladder carcinoma of this grade and stage, these survivals are considered significant, since recurrences generally appear within six months of radiotherapy and almost certainly within the first year. Marshall had no two-year survivals in untreated cases, reckoning from the date of diagnosis.

Radical therapy, whether in the form of supervoltage irradiation or radical cystectomy, is in order almost immediately. Although success can be achieved by more limited forms of therapy, surgical knowledge rather than clinical estimate of the staging should be relied upon. That is,

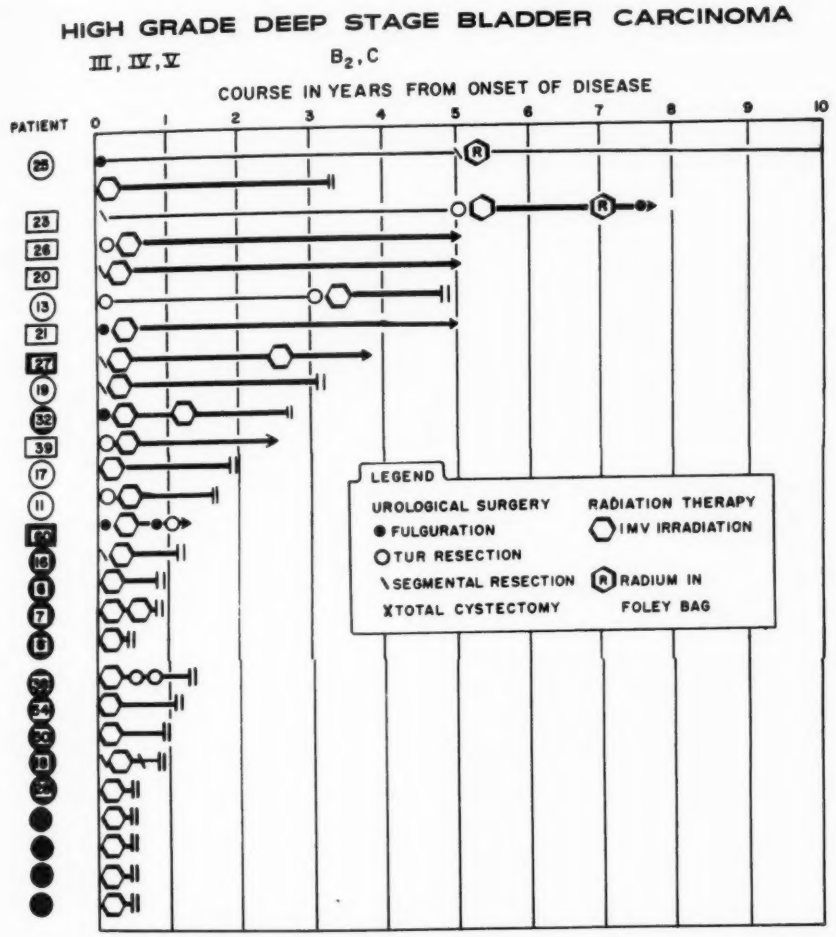

Fig. 8. Plot of cases in Group II indicating that most cases present with the more aggressive type of disease immediately.

interstitial radium and radioactive central sources should be inserted under direct vision *via* a suprapubic approach, as advocated by those experienced with this method (7). In the absence of direct inspection of the pelvic contents, one must bear in mind that 40 per cent of these patients have pelvic node involvement despite negative palpation, according to Marshall. Thus, such surgical procedures as deep fulguration and segmental resection are bound to be inadequate for a large number of these patients.

It is of interest to examine the mortality pattern in this group (Table II). Persistent carcinoma most frequently results in obstruction with associated pyelonephritis and uremia. Metastases—abdominal and pulmonary— contributed to death in only 2 cases. (This observation is based on clinical and not autopsy information.) Once again, the deaths attributed to treatment must be recognized; following either modality they must be regarded as failures despite control of the disease. Thus, of the 5 deaths without carcinoma, 2 were the results of radiation complications. One patient had a contracted bladder and a severe cystitis leading to ureteral obstruction and uremia following

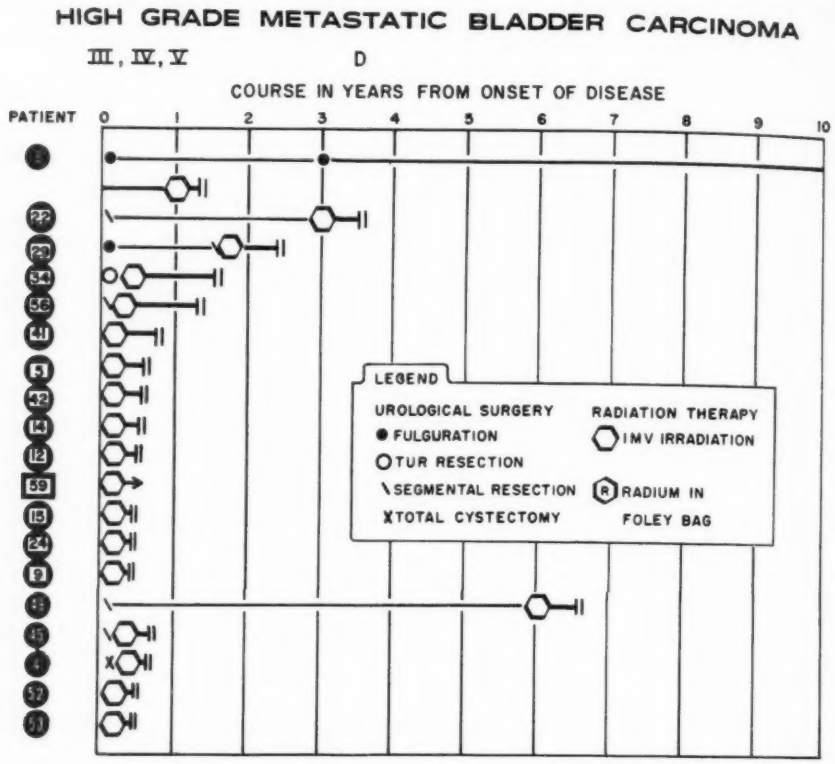

Fig. 9. Plot of cases in Group III showing the poor survival in this stage.

a repeat course of supervoltage irradiation. The other case was peculiar in that the patient was known to have telangiectatic veins for ten years prior to therapy, causing hematuria, which was repeatedly treated by fulguration. One year and nine months after irradiation, an uncontrollable bout of hematuria developed, due to a necrotic bladder ulcer, in the center of which was a dilated vein.

No real attempt is made to compare this series with those available in the surgical literature, since the criteria for classification differ. Thus Marshall's figures for two-year survival from date of treatment in deep-stage and high-grade lesions vary from 46 to 20 per cent, the lower figure once again representing those patients treated by more radical methods, and suggesting a factor of case selection and not the inadequacy of a more severe surgical approach. In all probability, those cases treated by more radical surgery are comparable to those included in our present series. The two-year survival figure without disease for our group is 37 per cent, which is most encouraging and indicates the merit of continued exploration of supervoltage irradiation in larger series to arrive at more meaningful figures. For a more detailed analysis of this group see Figure 8.

RESULTS IN GROUP 3

Metastatic Stage (*D*)	*High Grade* (*III, IV, V*)

The results in this group have been virtually *nil* with any modality of therapy, and supervoltage rotation therapy is no exception (Table III). No attempt at indicating control of the primary lesion is made, as autopsy follow-up is not complete enough. The high incidence of com-

TABLE III: BLADDER CARCINOMA: HIGH-GRADE (III, IV, V), METASTATIC STAGE

Total Number	19 cases
Curative Therapy	13 cases

	Without Disease	With Disease
Alive	0	1
Dead	0	12
TOTAL	0	13

Total Without Disease	0
Cause of Death in	18 cases
Persistent carcinoma	18 cases
Uremia	13
Metastases	6
Cardiac	1
Anemia	1
Without carcinoma	0 cases

plications and morbidity, as dysuria, severe cystitis, ureteral obstruction, contracted bladder, and acute retention suggests some problems of management in these patients. Death due to uremia is extremely common and shortens the patient's course. Perforation and fistula may occur. The courses of individual patients are graphed in (Fig. 9).

It would seem that some diversionary measure of transplanting the ureters to an ileal bladder (Fig. 10) might be equally or more palliative than moderate doses of irradiation. There is little doubt that in selected cases this lowers the morbidity of intensive irradiation and may mean the difference between delivering a palliative or curative dose. Not uncommonly, the more anaplastic tumors prove to be very radiosensitive and good responses can be obtained, with occasional sterilization of the primary lesion.

TABLE IV: IMMEDIATE RESPONSE TO THERAPY

	Total	Group I	Group II	Group III
Good	33 (54%)	10	18	5
Fair	14 (23%)	4	4	6
Poor	14 (23%)	2	4	8
TOTAL	61	16	26	19

RADIATION REACTIONS

The results of treatment depend upon achievement of the objectives outlined for therapy, namely, control of the neoplastic process without serious injury to normal structures. The complications secondary to treatment may be listed as early and late. Tabulated information on the immediate response in regard to tumor regression and the immediate unfavorable reactions at the conclusion of therapy is presented (Tables IV and V).

TABLE V: IMMEDIATE REACTION TO IRRADIATION

	Total	Group I	Group II	Group III
Diarrhea, mild	10 (16%)	3	3	4
Diarrhea, severe	4 (7%)	0	1	2
Cystitis, mild	25 (40%)	7	7	11
Cystitis, severe	9 (15%)	3	4	2

A good immediate response implies objective evidence of tumor regression and relief of distressing symptomatology, as hematuria and pain at the conclusion of treatment. Slow clearing of dysuria, frequency, and nocturia are not reliable indices of response, as they may reflect radiation cystitis. By a fair response, one infers good subjective evidence of control or relief of pain, cessation of hematuria but suggestive cystoscopic evidence of some residual tumor. Persistence of gross tumor with little subjective relief represents a poor result, not only from a curative but a palliative point of view.

Early or Acute Changes: (*a*) Radiation cystitis is the commonest untoward reaction, occurring in 55 per cent of our cases. It seems to be unrelated to the stage of the disease or dosage either on a daily or total dose level. Within four to six weeks of the end of therapy symptoms usually subside. This has been observed by others (7), although the frequency of this complication increases with the employment of larger doses and repetition of treatment. Secondary considerations, as associated infection, limited bladder capacity, frequency, and retention, heighten the mucosal reaction. Such agents as Pyridium and Banthine abet symptomatology, and careful selection of antibiotics is necessary to avoid the development of resistant bacterial strains. As a rule, Gantrasin is employed in acute exacerbations until culture studies and sensitivities are obtained. Instillation of topical solutions has been less successful. If

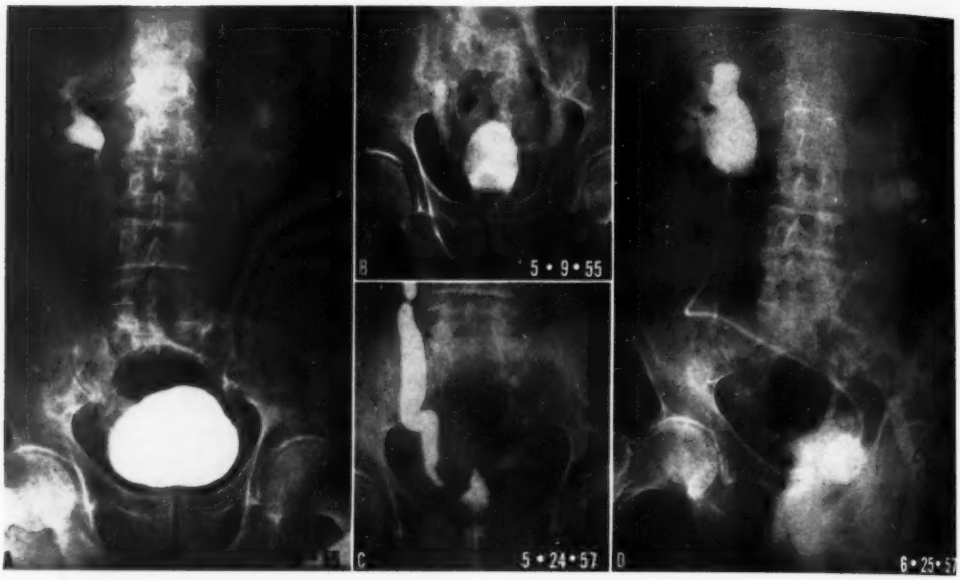

Fig. 10. Case No. 27: A. 1/11/55. Presented as a Stage C, Grade IV carcinoma with adequate bladder capacity. B. 5/9/55, two months after the completion of 6,000 r in six weeks. Note the decreased bladder capacity and bilateral hydronephrosis. C. 5/24/57. Severely contracted bladder with bilateral hydronephrosis. D. 6/25/57. Diversion required and performed *via* cutaneous ureterostomies.

the reaction is very severe, therapy may be interrupted or discontinued, more often by the patient than the radiotherapist. The severe form of this complication—persistence up to three months or longer—occurred in 14 per cent of our cases.

(*b*) *Ureteral obstruction* with uremia and fulminating pyelonephritis may occur during therapy. This usually takes place during the third or fourth week or later and corresponds to the onset of cystitis. Pyelograms early in the development of this process show narrowing at the vesicoureteral junction, with a tapered appearance to the ureter. Hydronephrosis and eventual atrophy will develop if a diversionary procedure is not instituted in time.

(*c*) *Perforation or fistulas* may result when supervoltage irradiation follows previous surgical or intense radiation therapy. Following segmental resection or extensive fulguration down to the serosa, recurrent tumor, if destroyed by irradiation in a zone where healing of normal tissues is poor, may lead to fistula formation. Perforation and fistualization rarely occur, if at all, as a direct effect of irradiation in normal zones of bladder tissue. This complication, in our experience, is more frequent in cases treated with orthovoltage (280 kv) therapy than with supervoltage.

Late Changes: (*a*) *Persistent cystitis:* A contracted bladder with limited capacity means persistence of frequency and nocturia (Fig. 10). This phenomenon is not only directly related to dose but duration and extension of the disease and associated infection add to this complication. In severe cases, the most effective measure to achieve palliaton is diversion of the urinary stream. If this complication is uncorrected, secondary pyelonephritis, uremia, and death occur.

Any therapy prior to an extensive course of irradiation heightens the possibility of a contracted bladder. A repeat course of radiation therapy to curative levels is almost sure to produce this complication, as demonstrated in one of our cases. The question of retreatment under any conditions, even to palliative levels, should be

carefully considered. Under no circumstances should it be done without histologic proof, since recurrent hematuria or a palpable mass (due to perforation and inflammation) may be late radiation reactions, and one would be adding further insult to injury.

(*b*) *Calculi* form in necrotic tumor and may be passed in the post-irradiation period. Occasionally, acute retention takes place in their passage, as was demonstrated in one of our cases.

(*c*) *Hemorrhage*, which follows months after therapy, may be due to atrophic and telangiectatic changes in the bladder mucosa secondary to radiation. If it is severe, clots may form, with bouts of acute retention requiring repeated catheterization.

In conclusion, a list of major complications (that is, contributing to the patients' death) in this series (Table VI) shows that

TABLE VI: MAJOR COMPLICATIONS AS A RESULT OF SUPERVOLTAGE IRRADIATION

1. Persistent cystitis (6 mos.)*	2
2. Ureteral obstructoin and 2° pyelonephritis*	1
3. Contracted urinary bladder	3
4. Ulceration and hemorrhage	1
TOTAL PATIENTS	4 (7%)

*Patient listed in 3 also.

7 per cent of the cases (4 of 61) were involved. This is less than the 14 per cent incidence (6/44) of deaths due to kidney complications following simple cystectomy for deep tumors as listed by Jewett. It should be recognized that need for ureteral transplantation, although listed as an occasional complication by radiation therapy, occurs in 100 per cent of the cystectomy cases. It may be pointed out once again that the good results and the complications must be measured against the same yardstick if a meaningful comparative analysis of surgical and radiotherapeutic technics is to be made in this disease.

ON UNIFORMITY IN REPORTING RESULTS

Recognizing fully that the small number of cases in each category of the series precludes the presentation of meaningful percentages, we include Table VII for the sake of uniformity with other authors.[3] The similarity in tabulation does not counterbalance the differences in case selection in surgical and radiotherapeutic series. The recorded percentages are based on those patients who are eligible for survival at the time indicated, who received curative irradiation. The most striking figure is in the percentage of patients surviving in the B_2 and C group. The higher survival percentage at five and three years as contrasted to two years is fortuitous and due to sampling. The two-year result is a truer representation of what our five-year figure might be with this method if a larger series were available for analysis.

TABLE VII: UNIFORM REPORTING OF BLADDER CARCINOMA
(61 Cases)

Stage	% Cases	Survivals 2 yrs.	3 yrs.	5 yrs.
0, A, B_1	27	45%	20%	0%
B_2, C	34	37%	40%	60%
D	22	0%	0%	0%
All cases	100	30%	18%	37%

CONCLUSIONS

The principles of treatment of bladder tumors are dependent upon the classification of each patient according to primary and secondary considerations.

1. *For Group I: Superficial-stage, low-grade carcinoma.*

(*a*) The initial treatment of choice is a conservative surgical measure such as fulguration, transurethral resection of tumor, or segmental resection.

(*b*) As the lesions recur, become multiple in origin, and change their histologic grade and depth of invasion, more radical measures are justified.

(*c*) Supervoltage irradiation should be employed only as an alternative to total cystectomy and not as a prophylactic measure.

[3] General agreement following discussion of the problem of reporting results in the literature with Dr. V. F. Marshall and Dr. M. Friedman, December 1958, in New York City.

2. *For Group II: Deep-stage, high-grade carcinoma.*

(*a*) Supervoltage irradiation in curative dosage levels has the most to offer patients with deeply invasive and aggressive carcinomas.

(*b*) Results suggest that cure rates are at least comparable and perhaps better than those obtained by radical surgical procedures, with less morbidity and mortality.

3. *For Group III: Metastatic-stage, high-grade carcinoma.*

(*a*) Supervoltage irradiation as a palliative agent can control pain and hematuria and is more easily tolerated than orthovoltage therapy.

(*b*) A diversionary measure, as an ileal bladder and ureteral transplantation, may be equally or more palliative in many cases than moderate doses of irradiation.

(*c*) In selected cases an ileal bladder may enable one to deliver a curative dose of irradiation and perhaps sterilize the primary lesion.

4. Last and of most importance is *cooperation* (*a*) between the patient and the physicians responsible for treatment and follow-up; (*b*) between the urologist and the radiologist, since in a large number of patients more than one modality of treatment will be utilized.

ACKNOWLEDGMENT: To Dr. Robert Bloor and Dr. Andrew Adams, my predecessors, who meticulously planned the treatment in most of the cases of bladder carcinoma reported; to Dr. Roger Terry, Associate Professor of Pathology, who painstakingly reviewed all of the pathological sections for proper classification and supplied the microsections for reproduction; to members of the Urology Department at all levels, for their kind cooperation.

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SUMMARIO IN INTERLINGUA

Irradiation a Supervoltage in Carcinoma del Vesica: 1952–1958

Le principios del tractamento de tumores del vesica depende del classification del patientes super le base de consideratione primari e secundari.

1. *Pro Gruppo I: Carcinomas de basse grado in stadio superficial.*

(a) Le tractamento de election es initialmente un mesura chirurgic conservatori, i.e. per exemplo fulguration, resection transurethral, o resection segmental.

(b) Quando le lesiones recurre, deveni multiple in origine, e altera lor grado histologic e le profundor de lor invasion, mesuras plus radical es justificate.

(c) Irradiation a supervoltage deberea

esser empleate solmente como alternativa pro cystectomia total e non como mesura prophylactic.

2. *Pro Gruppo II: Carcinomas de alte grado in stadio profunde.*

(a) Irradiation a supervoltage a nivellos de dosage curative offere plus que omne altere procedimento a patientes con carcinomas profundemente invasive e aggressive.

(b) Le resultatos assi obtenite pare indicar que le cifras de curation es al minus comparabile e forsan superior a illos obtenite per chirurgia radical, e le morbiditate e mortalitate es plus basse.

3. *Pro Gruppo III: Carcinomas de alte grado in stadio metastatic.*

(a) Irradiation a supervoltage como agente de palliation pote stabilisar le dolor e le hematuria e es tolerate plus prestemente que un therapia a orthovoltage.

(b) Un mesura diversionari—i.e. per exemplo un vesica ileal e transplantation ureteral—pote esser de valor palliative equal o superior a moderate doses de irradiation in multe casos de iste genere.

(c) In seligite casos, un vesica ileal permitte le application de un dose curative de irradiation e possibilemente le sterilisation del lesion primari.

Del plus grande importantia es le cooperation (a) inter le patiente e le medicos responsabile durante le tractamento e le periodo de observation posttherapeutic e (b) inter le urologo e le radiologo, proque in un grande numero de patientes plus que un modalitate de therapia debe esser utilisate.

DISCUSSION

Papers by Friedman and Rubin and Buran

Morton M. Kligerman, M.D. (New Haven, Conn.): I would just like to make one or two comments on the papers as presented.

Dr. Friedman has indicated that recurrences treated by high-dose methods do not do as well as cases treated primarily. This may be due to the fact that, as the disease progresses in an individual, the tumor-host relationship may change. At a late stage, therefore, even in a case primarily treated by irradiation, life expectancy may not be longer than in the recurrent case. If one would plot the survival in each case from the first treatment, whether it be surgery or radiotherapy, one might end up with a similar answer.

I do not know how Dr. Friedman delivers the high doses he reports. Perhaps this is a philosophical question in that I am unwilling to permit the development of severe complications if I can avoid them. I am not certain, when such complications develop, that the treatment indeed represents something worthwhile to the patient.

It seems to me that bladder carcinoma is an area to which the radiologist should turn his careful attention. In doing so, he will have to go beyond the excellent technics that both our essayists and others before them have demonstrated, possibly by sensitizing or augmenting the effects of radiation by chemicals. Radical surgery, as suggested by Dr. Rubin, has been disappointing. Dr. Marshall states that in 40 per cent of his cases, beyond grade I papillary tumors, there is involvement outside of the immediate vicinity of the bladder. One is caught, therefore, between exposing a large volume to a low dose with a low percentage of long survivals, in those patients with sensitive tumors, and perhaps giving better palliation during survival to a greater number of individuals by a higher dose limited to the bladder.

Radical surgery has not accomplished what had been hoped for it. Excellent methods for radiotherapy have been exploited, using the technics that you have seen today as well as others. I feel that this is an area in which augmentation of the effect of radiation should be investigated, with the use of drug therapy of some type. Perhaps, in utilizing the oxygen effect, we as radiotherapists have an opportunity of increasing the survival rate. Such an increase, I feel, is not open to surgery.

Spinal Sarcoidosis[1]

ERNEST H. WOOD, M.D., and CHARLES A. BREAM, M.D.

SARCOIDOSIS IS A relatively benign and indolent granulomatous disease of uncertain etiology occurring in young persons. Involvement of almost every organ has been described. Neurological lesions are relatively infrequent and the spinal cord is affected less often than the brain. It is the purpose of this paper to list reported information concerning spinal sarcoidosis, to describe an example of involvement of the spinal cord, and to show how myelography may be useful in establishing the diagnosis.

INCIDENCE AND PATHOLOGY

The true incidence of involvement of the nervous system in sarcoidosis is difficult to determine. Some portion of it is probably affected in approximately 1 per cent of patients (Ricker and Clark, 14; Höök, 7). Transient meningeal reactions without neurologic symptoms and signs, as manifested by cerebrospinal fluid changes, may occur much more frequently as a part of the generalized systemic reaction (Pennell, 12; Harrell and Fisher, 6). Disorders of the spinal portion of the central nervous system from focal intramedullary or extramedullary meningeal lesions are apparently very unusual. Verified examples of spinal cord involvement in sarcoidosis are rare (Table I).

The gross pathologic changes of sarcoidosis of the central nervous system usually are manifested as a leptomeningitis and less frequently as intracerebral or intramedullary granulomata (Longcope and Freiman, 10). The leptomeninges at the base of the brain are most commonly affected. Neural parenchyma may be involved by direct extension from the meninges. Often cranial and spinal nerves become diseased. In the few examples of spinal sarcoidosis studied at necropsy, the meningeal changes in the vertebral canal were found to be similar to those commonly encountered in the basal cisterns, and granulomatous extension into the spinal cord was demonstrable (Longcope, 9; Erickson *et al.*, 4; Aszkanazy, 1; Jefferson, 8).

Microscopically the central nervous system lesions of sarcoidosis are found to arise in perivascular spaces of the meninges. The arachnoid is infiltrated by lymphocytes, and granulomatous nodules become attached to the adventitia of small meningeal vessels (Aszkanazy, 1). The nodules are similar to sarcoid lesions occurring elsewhere in the body and consist of epithelioid cells, lymphocytes, plasma and other round cells, and giant cells, with varying degrees of fibrosis. The spinal lesions have been said to be less intense than those more commonly encountered at the base of the brain (Erickson *et al.*, 4). Meningeal lesions alone may result in vascular insufficiency and atrophy of neural tissue. In acute cases, meningeal vascular changes may lead to thrombosis and infarction (Meyer *et al.*, 11).

Within the neural substance perivascular infiltrations similar to the meningeal lesions may be present, especially in the subependymal layer. In the deep neural lesions only a few giant cells and round cells may be found attached to very small vessels, and occasionally a few such cells are free in nervous tissue without vascular attachment. When a portion of the nervous parenchyma becomes infiltrated by granulomatous nodules, the neural elements are destroyed directly, and degeneration of nerve tracts and atrophy of stroma result. Gendel and associates (5) also attributed demyelinization in the absence of other spinal cord changes to sarcoidosis.

[1] From the Department of Radiology of the School of Medicine, the University of North Carolina, and the Radiological Service of the North Carolina Memorial Hospital, Chapel Hill, N. C. Accepted for publication in September 1958.

TABLE I: REPORTS OF VERIFIED EXAMPLES OF SPINAL CORD INVOLVEMENT IN SARCOIDOSIS

Cases	Authors	Level of Involvement	Lesions Present	Remarks
1	Longcope (1941)	Cervical	Myelitis and meningitis	Clinical manifestations of generalized sarcoidosis. At necropsy spinal cord and meningeal involvement said to be present but description not given.
2	Erickson *et al.* (1942)	Cervical Thoracic Lumbar	Myelitis and meningitis	Multiple systems involved. Patient died of recurrent hydrocephalus after operative intervention for basilar adhesive arachnoiditis. Gross appearance of spinal cord was normal but microscopic examination revealed scattered parenchymal infiltration of sarcoidosis.
3	Aszkanazy (1952)	Thoracic	Myelitis and meningitis	Upper thoracic spinal cord primarily affected. Extensive cervicothoracic laminectomy revealed a small spinal cord without gross evidence of disease. Necropsy disclosed an atrophic spinal cord which was diffusely infiltrated by small granulomatous nodules with cellular composition characteristic of sarcoid lesions. Leptomeninges were similarly infiltrated with granulomatous nodules attached to the adventitia of small blood vessels.
4	Jefferson (1957)	Cervical	Myelitis and meningitis	Cervical spinal cord compression syndrome the primary manifestation of disease. Laminectomy disclosed an intramedullary mass which was biopsied. Patient died one week after operation following a convulsive seizure. Microscopic examination revealed the tissue to be a typical sarcoid granuloma.
5	Wood and Bream (present report)	Thoracic Lumbar	Meningitis	Primary clinical manifestations the result of lower spinal cord and cauda equina meningeal involvement. Diagnosis of arachnoiditis established by myelography. Recovery following lysis of adhesions and cortisone therapy.

PRIOR INVESTIGATIONS

An early report of the clinical manifestations of spinal sarcoidosis was given by Critchley and Phillips (3) in 1924. The authors described a patient with uveoparotid fever in whom neurologic signs of a low cervical spinal cord lesion developed during the course of the disease. A number of examples of similar neural involvement, diagnosed clinically, have been recorded subsequently (Reisner, 13, 1944; Colover, 2, 1948; Pennell, 12, 1951).

Histologically verified examples of spinal cord involvement in sarcoidosis are singularly scarce in medical literature. A pathologic study of a patient with extensive disease of the central nervous system, including the spinal cord, was reported by Erickson, Odom, and Stern (4) in 1942 (Case 2, Table I). The patient died of obstructive hydrocephalus resulting from chronic adhesive arachnoiditis at the base of the brain, and autopsy showed parenchymal infiltration of the brain stem and spinal cord to be present also.

A classical example of spinal sarcoidosis was studied at necropsy by Aszkanazy (1) (Case 3, Table I). Symptoms and signs were indicative of an upper thoracic spinal cord lesion, but surgical exploration disclosed only an atrophic spinal cord. The patient remained bedridden and died six years later of inanition. Postmortem study revealed both myelitis and meningitis, with diffuse infiltration by granulomatous nodules throughout the thoracic region. The diagnosis was not suspected during life.

More recently Jefferson (8) has recounted the history of a patient whose primary clinical manifestations were due to a parenchymal granuloma of the cervical spinal cord (Case 4, Table I). Clinically, myelographically, and at laminectomy the lesion was indistinguishable from an intramedullary tumor. Examination of the surgical specimen and subsequent necropsy

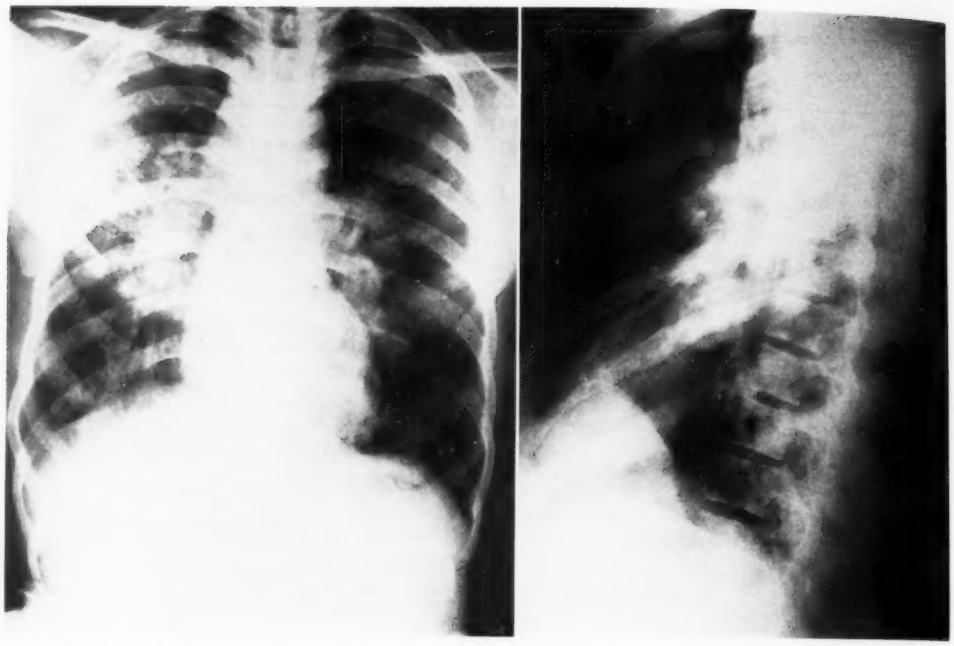

Fig. 1. Sarcoidosis of the lungs and mediastinal lymph nodes. Multilobular lymphadenopathy of the mediastinum and lung roots is present and enlarged intrapulmonary nodes extend along the paths of the vascular trunks. Coarse interstitial pulmonary infiltration is present, particularly in the right upper lobe, and numerous small nodular shadows are scattered throughout both lungs.

revealed that the spinal cord tumor was a sarcoid and that generalized sarcoidosis was present, even though many lesions were microscopic.

In one of the cases previously reported (Case 1) the patient apparently died of disease primarily involving vital organs other than the central nervous system, and neural involvement was an unexpected necropsy finding. One patient (Case 2) had a cerebral lesion as the most important manifestation of sarcoidosis, and the spinal involvement was discovered incidentally at necropsy. In 2 patients (Cases 3 and 4) the only clinical evidence of sarcoidosis was referable to the spinal cord, although necropsy demonstrated numerous other lesions of this generalized disease.

The case to be described here (Case 5, Table I) resembles Cases 3 and 4 in that the chief manifestations of sarcoidosis resulted from the spinal lesions. In this instance an arachnoiditis rather than an intramedullary lesion was present. As far as has been determined, radiologic findings leading to the diagnosis and definitive treatment of spinal sarcoidosis, with recovery, have not been described. The following case should therefore be of interest.

REPORT OF CASE

A 24-year-old man was admitted to the hospital because of weakness of the legs of two weeks duration. He had experienced pain in both lower extremities periodically for approximately eight months. This was of an aching character, was not of constant distribution, and occurred at irregular intervals. Six weeks before admission it began to occur more frequently, and two weeks before admission had increased in severity and become constant. At the same time numbness and coldness of the legs and feet developed. The legs became weak and for several days before entering the hospital the patient was unable to walk.

Nine months previously the patient had been referred to the hospital because of an abnormal finding on a miniature chest film made during a public health survey study. At that time he was asymptomatic, and the only significant finding on physical

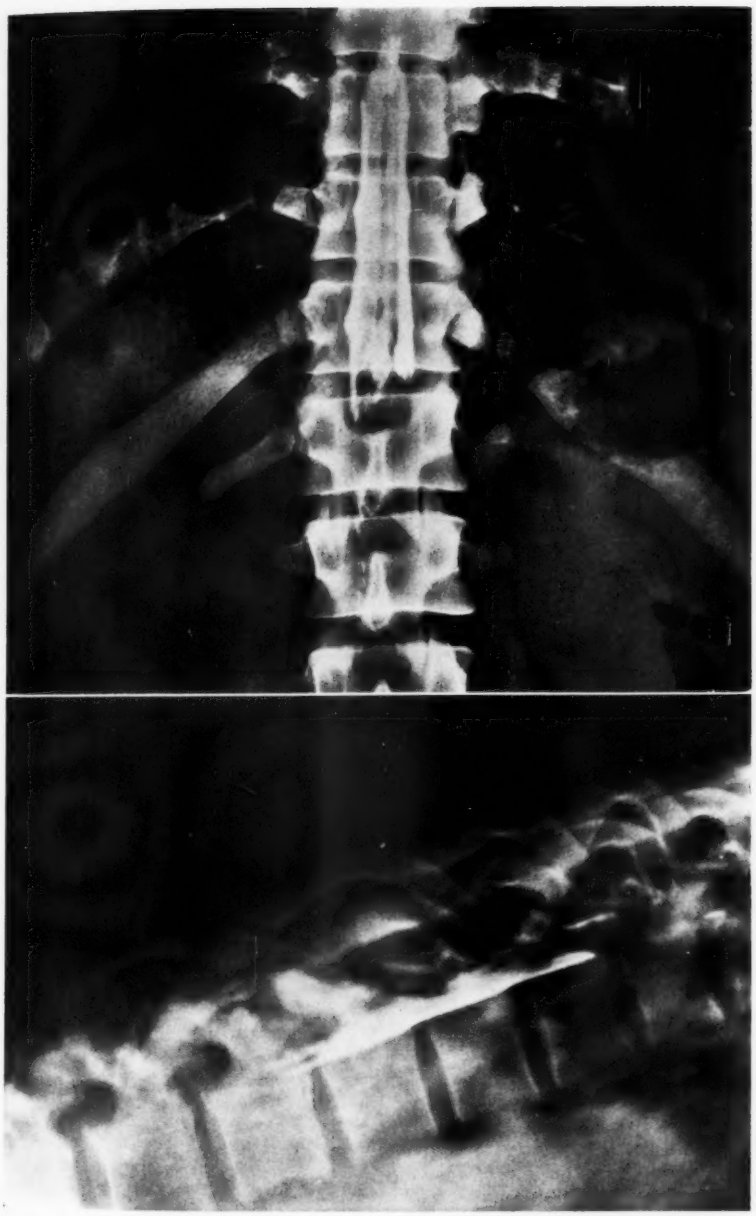

Fig. 2. Arachnoiditis of the spinal meninges producing obstruction to the caudad passage of Pantopaque at T-12 following cisternal injection. The head of the oil column is irregular, and there is no evidence of intramedullary or extramedullary tumor. Several droplets and linear collections of contrast material extend below L-1. (See Fig. 3).

examination was a bilateral uveitis and pearly white infiltrates along the course of the choroidal vessels seen on ophthalmoscopic examination. No enlarged superficial lymph nodes were present for biopsy.

On admission, a flaccid paraparesis was present,

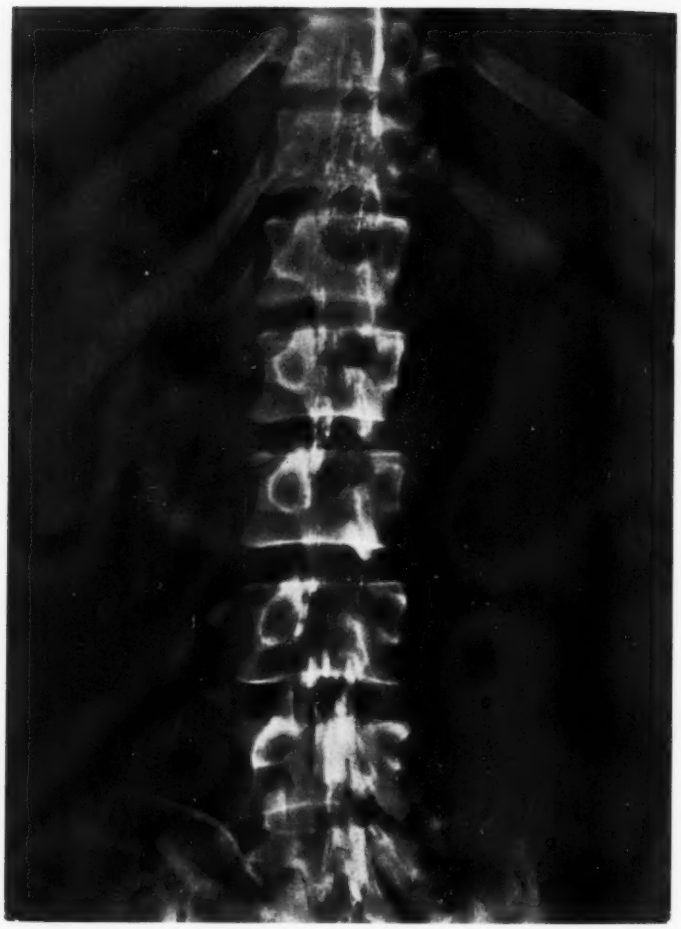

Fig. 3. Delayed roentgenogram after cisternal Pantopaque injection, demonstrating arachnoiditis in sarcoidosis. The main body of contrast material has descended to the sacral cul-de-sac with trailing linear and globular pocketed residues of Pantopaque extending from T-10 to the sacrum. In the lower lumbar region the outlines of the cauda equina filaments are widened, an appearance which usually results from adherence of nerve roots.

with absence of the deep tendon reflexes of both lower extremities. Superficial reflexes were preserved and normally active. There were hypalgesia and hypesthesia on both sides, in the distribution of the dermatomes below L-5. Vibratory sense and position sense were impaired bilaterally.

Chest roentgenograms revealed mediastinal and intrapulmonary lymph-node enlargement which was discretely multinodular and fairly symmetrical (Fig. 1). A large right paratracheal node was evident and the intrapulmonary nodes near the lung roots were enlarged along the courses of the main vascular trunks. Multiple examinations of the sputum and skin tests for tuberculosis and fungous diseases were negative. Laboratory examination revealed a normal leukocyte count but there were 9 per cent eosinophils. The total serum protein was 7.0 gm., with a reversal of the A-G ratio (albumin, 3.4; globulin, 3.6). Blood calcium was elevated to 14.8 mg. per cent and the alkaline phosphatase was 21.9 mg. per cent. A positive Sulkowitch reaction was obtained in the urine. A clinical diagnosis of sarcoidosis was made at this time. Later a Kveim test was positive.

During the week following admission there was progression of the neurologic deficit, and signs indicative of spinal cord compression at T-10 developed. Lumbar puncture revealed a manometric block and a Pandy test of the very small quantity of fluid obtained was positive. Lumbar myelogra-

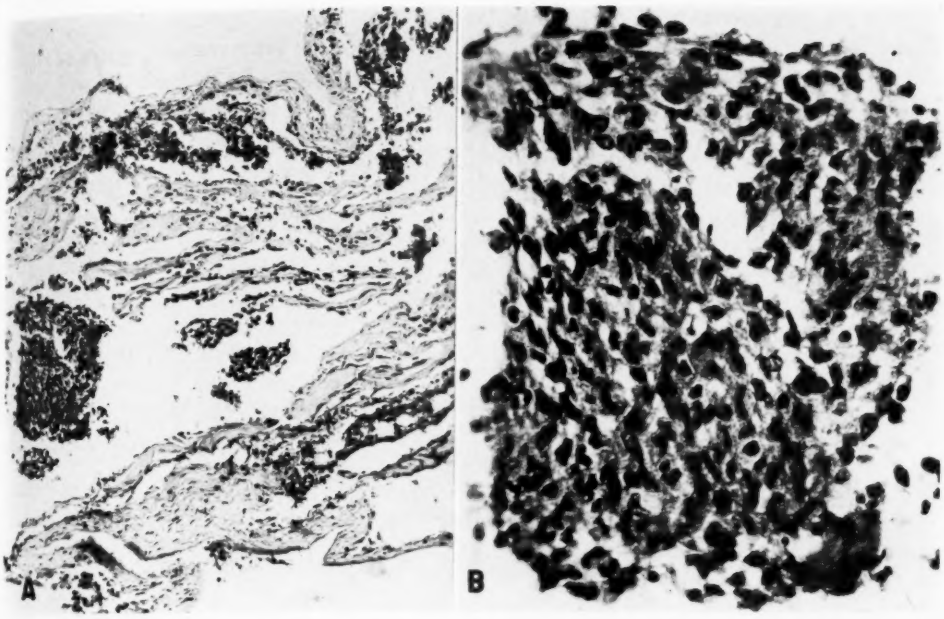

Fig. 4. A. Biopsy specimen of spinal arachnoid, containing a few lymphocytes and numerous compact aggregates of epithelioid cells, in which no necrosis is present. Multinucleated giant cells are neither numerous nor large. Hematoxylin and eosin. ×100

B. Higher magnification to show characteristic details of epithelioid cells, distinguishable from hyperplastic arachnoid cells by their nuclear configuration. Hematoxylin and eosin. ×400

phy had been planned, but the procedure was discontinued without instillation of Pantopaque. Three days later cisternal myelography was performed, revealing a subtotal obstruction to the caudad passage of the opaque material at the upper margin of L-1 (Fig. 2). The subarachnoid space tapered gradually from T-12 to L-1. There was no evidence of tumor. Subsequently Pantopaque passed the point of temporary obstruction and reached the sacral cul-de-sac (Fig. 3). The overall appearance was indicative of adhesive arachnoiditis.

A bilateral laminectomy was performed from T-10 to L-1. The arachnoid was thickened and milky white. The roots of the cauda equina and the spinal nerve roots leaving the cord at vertebral levels T-10, 11, and 12 were adherent and fixed by a gelatinous adhesive process, but could be easily separated. A portion of the arachnoid was removed for histologic examination, and lysis of the nerve roots was accomplished. The spinal cord itself appeared normal and was not biopsied.

Examination of the biopsy specimen revealed loosely arranged, irregular bands of fibrous tissue in which there were scattered lymphocytes and many compact aggregates of epithelioid cells. Some cells were vacuolated, but no inclusions were seen. Caseation necrosis was absent, and no organisms were demonstrable. The histologic picture was that of chronic granulomatous reaction in the spinal arachnoid, consistent with sarcoidosis (Fig. 4).

Following operation the patient was placed on 300 mg. of cortisone (cortisone acetate, Upjohn) administered orally daily. After three weeks the daily dose was reduced to 150 mg. and during the following month the dosage was further decreased gradually. Muscle strength in the lower extremities returned rather rapidly, and with physical therapy the patient became ambulatory. The reflex abnormalities disappeared more slowly.

The patient was discharged seven weeks after operation and was continued on a daily dose of 50 mg. of cortisone. Five months following operation he walked well. All reflexes except the left Achilles tendon reflex had returned to normal, and there was only a small area of impaired sensation over the lateral aspect of the left foot. The patient has remained essentially well for two and a half years. He pursues his occupation of farming, working almost as energetically as before his illness.

It is of interest that the patient's monozygotic twin has similar lymph node and some pulmonary involvement but is asymptomatic. Thus far, the brother's disease has been limited to the chest.

COMMENT

While sarcoidosis is characterized by spontaneous remissions, central nervous

system, cardiac, renal, and ocular involvement are usually considered definite indications for treatment. In the instance reported here, spinal cord compression developed during a period when the disease in other organs was not clinically manifest. Under such circumstances it is important to establish, if possible, the nature of the neural lesions before treatment is instituted, since a choice between medical and surgical management exists. Myelography is the logical procedure to identify disease processes producing mechanical effects upon the spinal cord.

Different organs involved in sarcoidosis often respond variously to steroid therapy. The small number of patients with neural involvement treated in this manner does not allow satisfactory assessment of such treatment. In the one case with symptoms of a spinal cord lesion described by Siltzbach (15), which was treated with cortisone, no alteration of the neurologic signs was produced.

The chief effects of the granulomatous lesions are mechanical rather than toxic, and scarring is a conspicuous feature of the healing phase. As a result, decompressive surgery and lysis of adhesions may be necessitated in some instances. Because of the obscure nature of most cases of arachnoiditis, Erickson and associates (4) have advocated more frequent biopsies when adhesive meningeal changes are encountered.

The possible importance of familial factors in the development of sarcoidosis in siblings is well recognized (Swirsky and Lowman, 16). The presence of similar clinical manifestations in identical twins was not observed in this study. The twin brother's disease has thus far remained more mild in character, and the presence of sarcoidosis was established only by a specific clinical and radiologic search for the lesions. Neurologic examinations have disclosed no evidence of involvement of the central nervous system.

SUMMARY

1. Involvement of the spinal cord and its membranes in sarcoidosis occurs infrequently. Four verified cases of spinal sarcoidosis have been described previously. In these instances the diagnosis was made on pathologic evidence after operation or necropsy.

2. An example of sarcoidosis resulting in an arachnoiditis which produced mechanical effects on the spinal cord has been described. Myelography was used to establish the existence, location, and extent of meningeal involvement. After operative division of adhesions and the administration of cortisone the patient experienced almost complete functional recovery and has remained well for more than two years.

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SUMMARIO IN INTERLINGUA

Sarcoidosis Spinal

Le affection del medulla spinal e de su membranas per sarcoidosis es un occurrentia infrequente. Quatro verificate casos appareva previemente, e istos es summarisate brevemente. Le diagnose in omne iste casos esseva facite super le base de constatationes pathologic post le operation o post le necropsia. Es reportate un nove caso in que un arachnoiditis causate per sarcoidosis produceva effectos mechanic super le medulla spinal a un periodo quando le morbo non esseva clinicamente manifeste in altere partes del corpore. Le existentia, location, e extension del affection esseva establite per myelographia. Post le operation (que includeva le division de adhesiones) e un curso therapeutic a cortisona, le patiente experientiava un quasi complete restablimento functional, e al tempore del presente reporto ille se trova ben depost duo annos.

Un gemino monozygotic del patiente habeva lesiones sarcoide restringite al thorace, sed iste subjecto esseva asymptomatic.

Roentgen Diagnosis of Retrograde Jejunogastric Intussusception[1]

LESTER W. PAUL, M.D., and CHARLES BENKENDORF, M.D.

RETROGRADE JEJUNOGASTRIC intussusception is an infrequent complication of gastrojejunostomy and of gastric resection. Preoperative diagnosis on the basis of clinical signs and symptoms is difficult. High mortality is associated with the acute form of the disease if operative intervention is not accomplished within a short time after the onset. Therefore, roentgen gastrointestinal examination and a proper evaluation of the findings may be life-saving.

In 1948 Aleman (1) was able to find descriptions of 70 cases in the literature and added 2 of his own. Since then cases have been reported regularly and the total now probably exceeds one hundred.

The types of jejunogastric intussusception and their relative frequency according to Aleman are as follows:

Type I. Intussusception of the afferent loop (10 per cent)

Type II. Intussusception of the efferent loop (74 per cent)

Type III. Combined intussusception of both loops (16 per cent)

In Aleman's series, therefore, retrograde intussusception accounted for some three-fourths of the cases, and this ratio probably is true for those reported since that time.

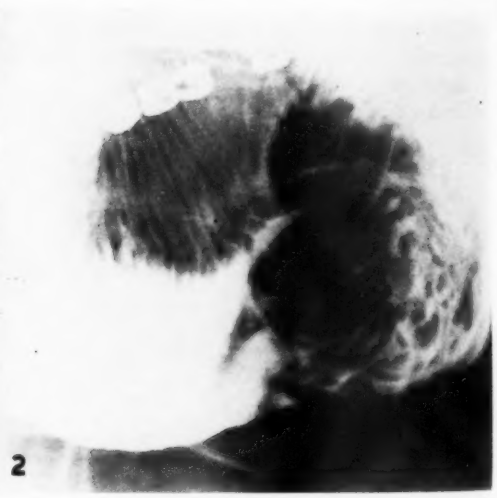

Fig. 1. The intussuscepted jejunum causes a filling defect in the stomach. The margins of the defect show the "coiled spring" appearance characteristic of stretched valvulae conniventes of the jejunum.

Fig. 2. Enlargement of a "spot" roentgenogram of the area of filling defect shown in Figure 1. This was made with compression during fluoroscopy and illustrates more clearly the coiled spring appearance indicative of jejunal mucosa.

Intussusception has been found most frequently after gastroenterostomy, though it has been reported occasionally as a complication of subtotal gastric resection. The much higher incidence after gastrojejunostomy has been explained on the basis of the frequency with which this procedure has been done in the past as compared with gastric resection. It has been suggested that in the future the con-

[1] From the Department of Radiology of the University of Wisconsin Medical School and University Hospitals, Madison, Wisc. Accepted for publication in October 1958.

dition will be found more frequently after gastrectomy. The cause of jejunogastric intussusception is unknown, however, and recently reported cases do not show a tendency for reversal of the trend (2–10). It is very possible that the factor or factors responsible for its development are more prone to occur after gastroenterostomy than after resection.

CASE REPORT

J. O., a 49-year-old white male, was admitted to the University Hospitals on Dec. 21, 1956, complaining of severe colicky abdominal pain. The pain was periumbilical in location. It began five days before admission and was associated with a feeling of fullness in the epigastrium. The patient could not retain food or liquids. He vomited bile-stained material and this gave some relief of pain. While hospitalized elsewhere, he was treated with nasogastric suction and parenteral fluids. There was no history of hematemesis or melena until after admission to this hospital, when there was one emesis of a small amount of bright red blood.

There was a long standing history compatible with the diagnosis of duodenal ulcer. The patient stated that the ulcer had perforated in 1940. He was operated upon at that time, the ulcer was closed, and a gastroenterostomy performed. There was a return of ulcer symptoms in 1951, consisting of pain before meals relieved by food intake. Symptoms recurred each Spring and Fall, and in August of 1956 the patient had an attack of severe periumbilical pain which was relieved only after vomiting of bile-stained material. This episode required hospitalization for seven days. A gastrointestinal roentgen examination was not performed at that time. An appendectomy was done in 1927 and an incisional hernia was repaired in 1935.

The pertinent physical findings were limited to the abdomen. In the epigastrium there was mild tenderness without associated spasm. The bowel sounds were high-pitched.

The day after admission a gastrointestinal series was done. This demonstrated a 10-cm. circumscribed filling defect arising from the postero-inferior surface of the pars media of the stomach (Fig. 1). Application of pressure over the defect revealed parallel curved lines (Fig. 2) having a coiled spring effect, representing barium-outlined valvulae conniventes. The duodenal bulb was deformed, and a slightly dilated duodenal loop was visualized. The barium did not pass beyond the region of the angle of Treitz and an efferent loop of a gastrojejunostomy was not seen (Fig. 3). A preoperative diagnosis of retrograde jejunogastric intussusception was made and confirmed at surgery two days later. The intussusception was reduced, and the intussusceptum did not appear gangrenous. The efferent loop of the gastroenterostomy, however, prolapsed easily through the stoma into the stomach for a distance of 12 to 15 cm. A subtotal gastrectomy with an antecolic gastroenterostomy was performed, and the patient made an uneventful recovery.

Fig. 3. Postero-anterior view demonstrating complete obstruction in the region of the gastroenterostomy stoma and persistence of the mass within the body of the stomach.

DISCUSSION

Jejunogastric intussusception occurs in two distinct clinical forms, the acute and the chronic. The acute type is characterized by an abrupt onset of severe colicky abdominal pain which is followed by vomiting, first of food and then of bile, and finally of blood. The patient may be in moderate to severe shock. According to Foster (6) a mass is palpable above and to the left of the umbilicus in over 50 per cent of cases. The prognosis is grave, and without surgery the mortality is said to be 100 per cent. Foster notes that, if the patient is operated on within forty-eight hours after the onset, the mortality is 10 per cent; if operation is delayed more than forty-eight hours the mortality is 50 per cent.

Gastrointestinal roentgen examination in cases of the acute type should establish

the correct diagnosis and thus indicate the need for prompt surgical intervention. In many instances surgical reduction of the intussusception is all that has been necessary, and the chance for recurrence apparently is slight. In other cases, because of the presence of gangrene, it has been necessary to resect the intussuscepted segment of jejunum. The roentgen findings consist in the visualization of a filling defect, which is rounded or sausage-shaped and is situated in the dependent part of the stomach. Characteristically, thin parallel curved stripes of barium can be seen over the surface of the mass, representing the stretched transverse mucosal folds of the jejunum. This feature is pathognomonic of intussusception. If the intussusception has occurred through a gastroenterostomy and the pylorus is patent, the barium mixture may be observed to leave the stomach and fill the afferent loop. This loop may be completely obstructed adjacent to the gastroenterostomy or the barium may be seen to enter the stomach but with no emptying through the efferent loop. The stomach may or may not be dilated. These roentgen findings, combined with the clinical observations, are so characteristic of intussusception that the diagnosis can be made with confidence.

The second clinical form of the disease is the chronic, recurring type. The clinical behavior is different than in the acute case, although the patient with chronic, recurrent intussusception is always a candidate for the development of an acute obstructive episode which may or may not be reversible. There is no characteristic clinical pattern for the chronic type of intussusception, but in most cases there has been a history of long standing difficulty following a gastroenterostomy, with epigastric pain, nausea, and vomiting occurring at irregular intervals. In some patients there apparently have been brief intermittent episodes of acute obstruction with spontaneous relief. In others, the clinical pattern has been of a more constant nature. Some authors have suggested that in many patients suffering from chronic gastrointestinal difficulties after a gastrojejunostomy the trouble actually may be due to recurrent intussusception with spontaneous reduction. Cases have been reported (4, 10) in which the roentgenologist has observed the occurrence of intussusception and noted its spontaneous reduction during fluoroscopy. The roentgen signs in chronic intussusception differ from the acute only in the tendency for the intussuscepted mass to be smaller and the possible demonstration of its spontaneous reduction or even its occurrence during fluoroscopy and manual palpation of the abdomen. The mass may be somewhat movable within the stomach. The parallel spiral folds of jejunal mucosa over the surface of the mass are highly significant. It is obvious that in many cases roentgen examination may reveal no abnormality unless by fortuitous circumstances the intussusception occurs during the examination. Also, a failure to find intussusception at the time of surgical exploration does not negate a positive roentgenologic study, because of the intermittent character of the intussusception in these cases. Whenever possible, roentgen examination should be performed at a time when symptoms are present, if they are episodic in nature.

SUMMARY

A case of retrograde jejunogastric intussusception is reported in which the preoperative roentgen diagnosis was confirmed at surgery. The clinical and roentgen manifestations of this interesting entity are reviewed.

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SUMMARIO IN INTERLINGUA

Diagnose Roentgenologic de Intussusception Jejunogastric Retrograde

Es reportate un caso de intussusception jejunogastric retrograde, vidite circa dece-duo annos post gastroenterostomia pro ulcere duodenal. Un examine gastrointestinal demonstrava un defecto de plenation que habeva su base al superficie inferior del parte medie del stomacho. Le application de pression supra le defecto revelava curvate lineas parallel con le apparentia de un resorto helicoide que representava le tendite plicas mucosal del jejuno. Esseva establite un diagnose de intussusception jejunogastric. Isto esseva sequite per un operation chirurgic.

SUMMARIO IN INTERLINGUA

Intussusception Jejunogastric

(*Pagina 238*)

Intussusception jejunogastric es un complication infrequente de gastroenterostomia. Illo pote esser satis serie pro producer alarmante symptomas clinic. Es reportate un caso in un patiente con un anamnese de mastectomia radical pro carcinoma e irradiation pro carcinoma del larynge a metastases pulmonar. Symptomas gastrointestinal suggereva laparotomia exploratori, e isto revelava le presentia de un bezoar in le stomacho sed nulle evidentia de infiltration maligne.

Un gastrojejunostomia antecolic esseva effectuate. Isto esseva sequite per duo dies de persistente vomito e distension abdominal. Le examine roentgenologic revelava un aspecto irregular, a vices spiral del plicas mucosal. In le radiogramma de octo horas le ansa afferente del anastomose pareva dilatate e redundante, con grados considerabile de retention in le stomacho e le bulbo duodenal. Nulle signo de medio opac esseva notate in le ansa efferente. Al operation il esseva constatate que le ansa afferente esseva patente e levemente dilatate. Le ansa efferente esseva collabite, e un segmento de omento adhereva circum le anastomose. Un grado moderate de intussusception del anastomosate jejuno a in le stoma esseva observate. Un associate volvulo del ansa efferente esseva constatate. Le patiente se restabliva immediatemente, sed ille moriva octo menses plus tarde, apparentemente ab cancere metastatic.

Jejunogastric Intussusception[1]

C. SOTEROPOULOS, M.D., Y. BERKMEN, M.D., AND JOHN H. GILMORE, M.D.

JEJUNOGASTRIC intussusception is a rare complication of gastroenterostomy and may be serious enough to produce alarming clinical symptoms. The following case, although it had a rather typical clinical course, presents a few interesting facets in respect to the x-ray findings and presurgical history.

REPORT OF CASE

A 55-year-old white male had undergone a right radical mastectomy for carcinoma eight years earlier. Later he was found to have carcinoma of the larynx with metastasis to the left lung, for which he received radiation therapy. His present admission was prompted by the occurrence of epigastric pain and some vomiting in the mornings.

An upper gastrointestinal tract study showed what appeared to be a bezoar in the stomach (Fig. 1), but no free acid was present. Repeated lavage and re-examination showed essentially the same findings. Exploratory laparotomy revealed a mass of undigested string beans in the stomach, adherent to the mucosa, which was relatively coarsened. No evidence of malignant infiltration was observed. An antecolic gastrojejunostomy was performed.

Two days following operation the patient vomited profusely, and vomiting continued for several days. Abdominal distention was relieved by gastric suction. Fluids were given intravenously. The temperature rose intermittently, but the general condition was satisfactory.

An x-ray study of the upper gastrointestinal tract approximately two weeks after the operation revealed a filling defect in the greater curvature of the stomach at the area of the anastomosis, with some edema of the gastric mucosa (Fig. 2). The mucosal folds had an irregular to occasionally spiral appearance. On the eight-hour film the afferent loop of the anastomosis appeared dilated and redundant (Fig. 3) with considerable retention in the stomach and duodenal bulb. There was no evidence of opaque medium in the efferent loop.

These findings suggested a diagnosis of jejunogastric intussusception, and surgical exploration was undertaken. The afferent loop was patent and slightly dilated. The efferent loop was collapsed, and a segment of the omentum was adherent about the anastomosis. A moderate degree of intussusception of the anastomosed jejunum into the stoma was observed. In addition, there was incomplete volvulus of the efferent loop. The obstruction was released and the patient made an uneventful recovery. He was discharged from the hospital the tenth postoperative day feeling well. He died at home eight months later, apparently from metastatic cancer.

Fig. 1. Multiple defects in the stomach due to proved bezoar.

DISCUSSION

Considering the frequency of gastric surgery, jejunogastric intussusception is a rare complication, or at least infrequently recognized, as indicated by the number of proved cases in the literature (about 100). Until 1948 only 12 cases were diagnosed roentgenographically.

The afferent loop, efferent loop, or both may be involved. The incidence is highest in the efferent loop, 74 per cent

[1] From the X-ray Department of the Illinois Masonic Hospital, Chicago, Ill. (J. H. G., Director; C. S., Associate Radiologist; Y. B., Resident in Radiology). Accepted for publication in October 1958.

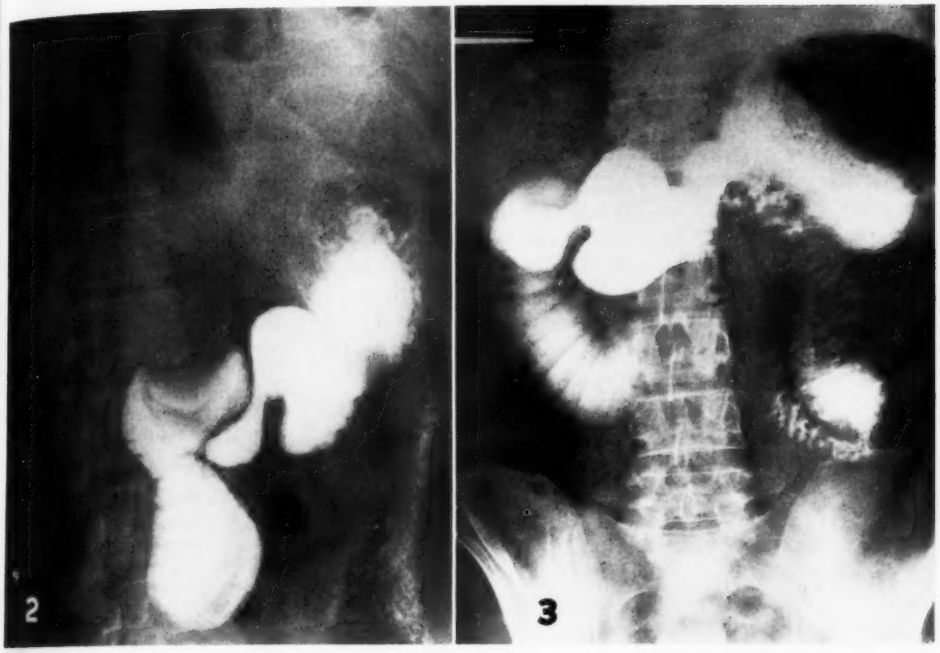

Fig. 2. Redundant afferent loop and defect at site of anastomosis.
Fig. 3. Dilated afferent loop of anastomosis. Retention of barium in stomach. Irregularity of mucosa at the anastomosis with spiral effect. Eight-hour film.

according to Aleman. In our case there was associated volvulus of the intussuscepted efferent loop with a part of the omentum interposed, a combination which has not been mentioned in the reported cases.

The clinical findings are not characteristic. The condition may appear with acute symptoms of sharp pain and vomiting, and occasionally a palpable mass, or there may be chronic recurrent complaints of indigestion and pain. In the acute type the symptoms may be dramatic, with sudden onset of epigastric pain and profuse vomiting, prostration, and hematemesis when gangrene of the involved segment occurs. Definitive diagnosis requires x-ray study.

The cause of the intussusception is not known, but several interesting speculations have been mentioned. Local spasm of the jejunum, leading to reverse peristalsis and its retrograde invagination, may possibly be responsible. The size of the stoma and/or iso- or anti-peristaltic anastomosis may be predisposing factors, but data on these points are inadequate in the reported cases.

Roentgen Diagnosis: A barium meal will show obstruction of the stoma with a mass protruding into the lumen of the stomach, producing a filling defect. The size of this defect will vary depending upon the length of the protruding jejunal segment, the amount of filling of the stomach, and the degree of pressure by the compression device. Also edema of the mucosa of the stomach is frequently seen. If the pressure exerted is too great, the mucosal pattern of the jejunum may disappear. An indentation of the wall of the stomach at the stoma is frequently seen, attributable to the mass of the intussuscepting loop and attached omentum.

Some of the barium may enter the intussusceptum and show the characteristic folds of the jejunum appearing as parallel curves, in a fan-shaped pattern, or as

spirals. Re-entry of the barium into the stomach by way of the afferent loop and stoma is occasionally observed.

If the efferent loop is involved, the afferent loop may fill partially and appear distended, with stasis of secretions shown by dilution of the barium. There is usually edema at the stoma, however, which prevents satisfactory filling of the afferent loop. In cases of simple gastroenterostomy, the afferent loop is usually filled through the duodenum and appears distended, as in the above presented case.

Plain films of the abdomen may show slight dilatation of the stomach with a fluid level and occasionally a soft-tissue mass at the anastomotic site due to edematous, thickened jejunum. These findings, however, are not specific.

Complete knowledge of the preceding surgical procedure, if available, is of great assistance to the radiologist during the examination of the stomach. In chronic cases the complaints are mild and recurrent, and x-ray study is less frequently obtained.

In some cases diagnostic evidence may not be present at the time of the x-ray examination because of spontaneous reduction. It is advisable to make the examination during a symptomatic period.

Differential Diagnosis: When the typical x-ray findings are present, the diagnosis is readily made. Occasionally, however, there is considerable edema at the stoma a few days after the operation, with complete obstruction, making a definite diagnosis difficult. Adhesions and omentum interposed between the transverse colon and the stoma present similar clinical and x-ray findings.

The afferent loop syndrome may cause difficulty, but in this case the efferent loop is patent.

Marginal ulceration and recurrent peptic ulcer may be difficult to differentiate clinically, but are demonstrable on x-ray study. The same is true for the rare condition of jejunocolic fistula with an inflammatory mass around the anastomosis.

Other conditions that may present a confusing clinical picture are: high small bowel obstruction, acute pancreatitis, and biliary tract disease.

SUMMARY

A case of jejunogastric intussusception is presented, with unusual associated findings.

The condition is reviewed briefly, and the x-ray and differential diagnosis are discussed.

NOTE: We are indebted to Dr. Carl F. Steinhoff for referring this case for study and permitting this report and to Dr. W. C. Bornemeier, the operating surgeon.

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(Pro le summario in interlingua vider le pagina 237)

Aberrant Pancreatic Tissue in the Stomach

DONALD R. ROONEY, M.D.[2]

OF THE BENIGN tumors of the stomach wall, aberrant or accessory pancreatic tissue is one which may possess a distinct characteristic, thus enabling the radiologist to suggest the correct diagnosis. Most radiologists are familiar with this entity, and there are probably unrecorded cases in which the exact diagnosis was made preoperatively. There is, however, a paucity of reported instances in which the correct diagnosis was suggested on the basis of the roentgenologic findings. It would seem, therefore, that these findings should be re-emphasized. The purpose of this report is threefold: (*a*) to discuss briefly aberrant pancreatic tissue; (*b*) to reiterate the roentgen findings of aberrant pancreatic nodules in the stomach; (*c*) to add 7 cases to those previously reported.

Aberrant pancreatic tumors have been found not only in the stomach, but also throughout the small intestine and the transverse colon, in Meckel's diverticula, in the mesentery, spleen, gallbladder, bile ducts, liver, and mediastinum. Approximately 70 per cent are located in the stomach (1) and, of these, 85 per cent are in the antrum or pylorus. About three-fourths of these gastric nodules lie in the submucosal layers and project into the lumen. The remaining 25 per cent lie in the deeper layers and are more difficult to detect. The theories of origin may be briefly summarized as follows: (*a*) a transplantation of a portion of the pancreas from its original site during embryonic development; (*b*) metaplasia of other glands during postnatal life; (*c*) an atavistic phenomenon, with reversion to lower animal forms which contain pancreatic tissue in other locations.

Palmer (2) in 1951 presented an extensive review of gastric heterotopic pancreatic tumors and discussed the 215 proved cases from the world literature. Since his report, at least 143 additional cases have been found in the international medical literature; only 9 of these appeared in the American radiologic journals, in two separate reports (3, 4). Other indications of the incidence of this lesion have been suggested by de Castro Barbosa and Waugh, who stated that at the Mayo Clinic aberrant pancreatic tissue is found in the abdomen about once in every 500 laparotomies. de Castro Barbosa and his associates also stated that this lesion was found in 1.7 per cent of their routine autopsies between 1939 and 1943.

The most common symptom usually ascribed to aberrant pancreatic tissue in the stomach is non-specific epigastric pain. Six of our 7 patients had this complaint. Seventy-five per cent of the patients that Palmer (2) evaluated for clinical data had some type of epigastric pain as the presenting symptom. Pyloric obstruction is probably the next most common symptom. This was present in 25 per cent of Palmer's adult patients, and 1 of our patients had symptoms suggestive of partial intermittent obstruction with occasional episodes of distention. Other signs and symptoms, less frequently encountered, include massive gastrointestinal hemorrhage, anorexia, weight loss, a palpable abdominal mass, or even symptoms of islet cell dysfunction. Neoplasia, cyst formation, or acute inflammatory change may also occur.

The radiologic findings in our 7 patients were strikingly similar, as illustrated in Cases 1 and 2 (Fig. 1). We were especially impressed with the constant location, size,

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Fig. 1. Radiographs of Cases 1, 2, 3, 5, and 7 showing aberrant pancreatic nodules in the distal gastric antrum. Films of the other 2 patients were strikingly similar to these. The numbers indicate the cases.

and configuration of the nodular filling defect which was demonstrated radiographically in all 7 patients. These findings are well outlined by Littner and Kirsh (4). There is a solitary, sharply demarcated, round or oval filling defect, which is usually immobile, though occasionally the nodule may prolapse enough to cause pyloric obstruction. The lesions as a rule measure 1 or 2 cm. in diameter and are located for the most part in the gastric antrum within 6 cm. of the pyloric orifice. The surrounding mucosa is uninvolved, while that overlying the nodule is thinned

out and smooth. There is no interference with peristalsis, and no spasm is present in the uncomplicated cases.

The distinctive characteristic usually present grossly—which we wish to emphasize—is the presence of a central pit or depression. This depression surrounds the orifice of the duct draining the aberrant pancreatic acini. This central duct was identified in the gross specimen from each of our 7 patients. It varies from 1 to 5 mm. in diameter, and from 2 to 10 mm. in length, and is centrally located with the opening at the center or summit of the nodule. As stated by Littner and Kirsh, the regular margins and central location

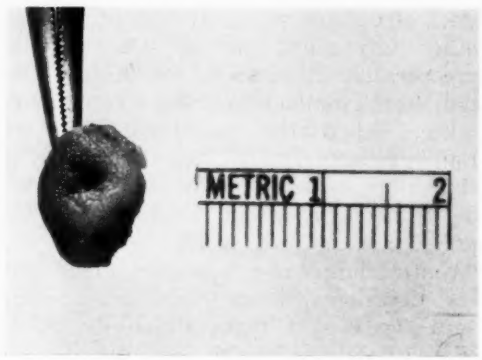

Fig. 2. Surgical specimen from Case 7, showing depression surrounding central duct orifice in aberrant pancreatic tissue.

TABLE I: SEVEN CASES OF ABERRANT PANCREATIC TISSUE

Case	Age and Sex	Symptoms	Size of Nodule	Size of Central Duct	Central "Dimple" Seen on Radiograph
1	61 F	Vague upper abdominal pain for several years	9 mm.	2 × 6 mm.	Yes
2	56 F	Intermittent pain under lower sternum for five years	18 mm.	Central duct present, size not stated	Yes
3	52 F	Upper abdominal distention and pain for six months	25 mm.	1 × 7 mm.	No
4	71 F	No gastrointestinal complaints	6 mm.	Central duct present, size not stated	No
5	53 F	Burning epigastric pain for a year and a half	10 mm.	2 × 6 mm.	Yes
6	64 M	Patient had symptomatic duodenal ulcer	Size not stated	8 mm.	Yes
7	32 M	Nausea and epigastric pain for five years	9 mm.	1 × 6 mm.	Yes

of this duct favor the diagnosis of aberrant pancreas over an ulcerated tumor, since in other extramucosal tumors, the ulceration would tend to be irregular and eccentrically located. In no other gastric tumor is there a structure comparable anatomically to the central duct of ectopic pancreatic tissue. In only 1 reported case (6) was a central dimple demonstrated in a small antral tumor which was later diagnosed as an adenomyoma, histologically resembling Brunner's glands. Our earlier cases were diagnosed, on the basis of the gross and histologic findings, as gastric diverticula plus ectopic pancreatic tissue. As we saw more of these lesions, it became apparent that the so-called diverticulum was in reality the central duct draining the pancreatic acini. This central duct was demonstrated radiographically and verified grossly in 5 of our 7 patients, and in 3 of the cases reported by Littner and Kirsh. In one of their cases, the correct preoperative diagnosis was suggested by a radiology resident, who was cognizant of the gross morphology of these lesions. In 2 of our patients, the correct diagnosis was also suggested preoperatively. In retrospect, this might have been possible in 4 of the remaining 5. These findings are summarized in Figures 1 and 2 and in Table I.

SUMMARY

Seven cases of aberrant pancreatic tissue in the stomach wall have been added to those previously reported. The distinguishing morphologic finding is a central

duct structure, which is not present in other intramural gastric tumors. The preoperative diagnosis on the basis of the radiologic examination is still a rare occurrence. When the radiologist finds a rounded sharply demarcated filling defect in the gastric antrum, measuring 1 or 2 cm. in diameter, a careful search, aided by pressure spot-films, should be made for a central dimple in this nodule. This central depression, when visualized, encourages the correct preoperative diagnosis. The visualization of this structure may be of great value to the radiologist and gastroscopist in the preoperative diagnosis; and to the surgeon or pathologist who may be confronted, in the operating room, with the decision of simple *vs.* radical gastric resection.

NOTE: The author wishes to express his appreciation to Lewis G. Norman, Jr., M.D., West Point, Georgia, for supplying the clinical information and surgical findings in Case 6 and to Ted F. Leigh, M.D., for preparing the photographs used to illustrate this report.

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SUMMARIO IN INTERLINGUA

Aberrante Histos Pancreatic in le Stomacho

Septe casos de aberrante histos pancreatic in le pariete del stomacho es addite a illos previemente reportate. Le distinctive constatation morphologic es un structura de ducto central que non occurre in altere tumores gastric intramural. Diagnoses preoperatori super le base de examines radiologic remane rar. Quando le radiologo constata un arrondate e nettemente demarcate defecto de plenation in le antro gastric con un diametro de inter 1 e 2 cm, le plus meticulose scrutinio es indicate pro le discoperta de un depression central in iste nodulo. Quando un tal depression central es visualisate, illo debe esser interpretate como supporto de un diagnose preoperatori de aberrante histos pancreatic in le stomacho. Le visualisation de iste structura deveni possibilemente de grande valor al radiologo o al gastroscopista in le diagnose preoperatori e etiam al chirurgo o al pathologo qui se trova, in le sala de operation, confrontate con le necessitate de facer le decision inter resection gastric simple e resection gastric radical.

Hip Arthrography in Children, with Renografin[1]

JAMES C. BARNETT, M.D., and JOSEPH P. ARCOMANO, M.D.

THE PURPOSE OF recording the present series of cases is to direct attention to the practice used in the St. Charles Hospital (Brooklyn, N. Y.) in the study of congenital dysplasia of the hip. Following the taking of the history and physical examination, routine films—anteroposterior and frog-lateral views—are obtained for every child suspected of having hip disease. It is then decided whether or not horizontal-lateral views will be helpful (1). Thereafter the decision as to the future management of the case is made. In many cases arthrography has been found to be an extremely useful guide to the clinician. Upon information thus obtained he may base his choice between closed and open reduction.

As a contrast substance Renografin (Squibb) has been found to be so innocuous and kind to the tissues that it was felt that it should be brought to the attention of others practicing arthrography. We have employed Renografin for several years, for most cases using a 20 per cent solution of the medium. Renografin contains in aqueous solution the solubilized salt of 3,5-diacetylamino-2,4,6-triiodobenzoic acid. We had previously been impressed by the extremely low toxicity of this solution both in intravenous pyelography and in work on laboratory animals, with particular respect to the peritoneal cavity and the eye.

The standard method of injection for hip arthrography may be used, but at the St. Charles Hospital we have employed the method described by Kubiak (2).

The quality of the opaque substance within the capsule of the hip joint has proved to be eminently satisfactory, providing definite information, verified at operation, regarding the uncalcified limbus, the thickness of the ligamentum teres, the fixation of the capsule to the ilium, the relationship of the uncalcified femoral head to the uncalcified limbus, the presence or absence of complete or partial dislocation, and the degree of hour-glassing of the capsule.

To date 49 hip arthrograms have been obtained. For 44 of these Renografin diluted to approximately 20 per cent was used. The group included 43 females, ranging in age from six weeks to ten years, and 6 males among whom were the youngest patient, aged two weeks, and the oldest, thirteen years. In only one instance—in a fourteen-month-old girl—was a systemic reaction observed. No local reactions were encountered.

It is to be noted that arthrography of the normal hip has produced no clinical signs or symptoms, though many of the patients have been followed as long as three years. The opaque material appears to be absorbed almost completely within the first hour. At times, absorption is even more rapid, having actually occurred in a period of about twenty minutes.

Prior to the adoption of Renografin as a contrast substance, another medium was employed, which caused a slight temporary systemic reaction, lasting for about an hour. Because of this, it is our policy to skin-test all patients prior to arthrography. This is usually done by a small intradermal injection of about 0.1 c.c. of the medium to be used.

The arthrograms reproduced in Figures 1 to 6 are illustrative of the procedure.

Figure 1 is an arthrogram of the right hip. The uncalcified limbus is clearly defined. The orbicular ligament is well delineated, and the uncalcified right femoral head fits tightly against the acetabulum, the floor of which is smooth and regular, permitting no significant amount of opaque substance to interpose itself between the femoral head and the acetabular floor.

[1] From the Department of Radiology, St. Charles Hospital, Brooklyn, N. Y. Accepted for publication in September 1958.

Fig. 1. Normal arthrogram of the right hip.
Fig. 2. Double arthrogram. Classical dysplasia of the right hip, with superior dislocation.

There has been a moderate amount of extravasation of the opaque substance into the soft tissues. This was interpreted as a normal arthrogram.

Figure 2 is a double arthrogram. It is apparent that the uncalcified left femoral head fits tightly into the acetabulum and the uncalcified limbus, while small, acts as an adequate shelf. There is no interposition of detritus in the base of the acetabulum. The right hip shows a classical dysplasia with superior dislocation. On the basis of the arthrogram, it can be stated that there are hour-glassing of the capsule, diminution in the size of the uncalcified femoral head, hypertrophy of the ligamen-

Fig. 3. Left arthrogram, showing features similar to those in Fig. 2, but with acorn-shaped femoral head.

Fig. 4. Bilateral arthrogram. Dysplasia of the combined type on the right, involving the femoral head and acetabulum, associated with complete lateral and superior dislocation. Widening of the hip joint space on the left, the so-called subluxation of Leveuf.

tum teres, moderate detritus in the floor of the acetabulum, probable fixation of the capsule to the ilium superiorly, and downward and inward projection of the uncalcified limbus, constituting what Leveuf (3) would designate as the luxated hip.

Figure 3, a left arthrogram, demonstrates almost all of the classical features seen in Figure 2. The uncalcified femoral head on the left, however, appears to be somewhat acorn-shaped, and this was verified at surgery. In addition, the size of the ligamen-

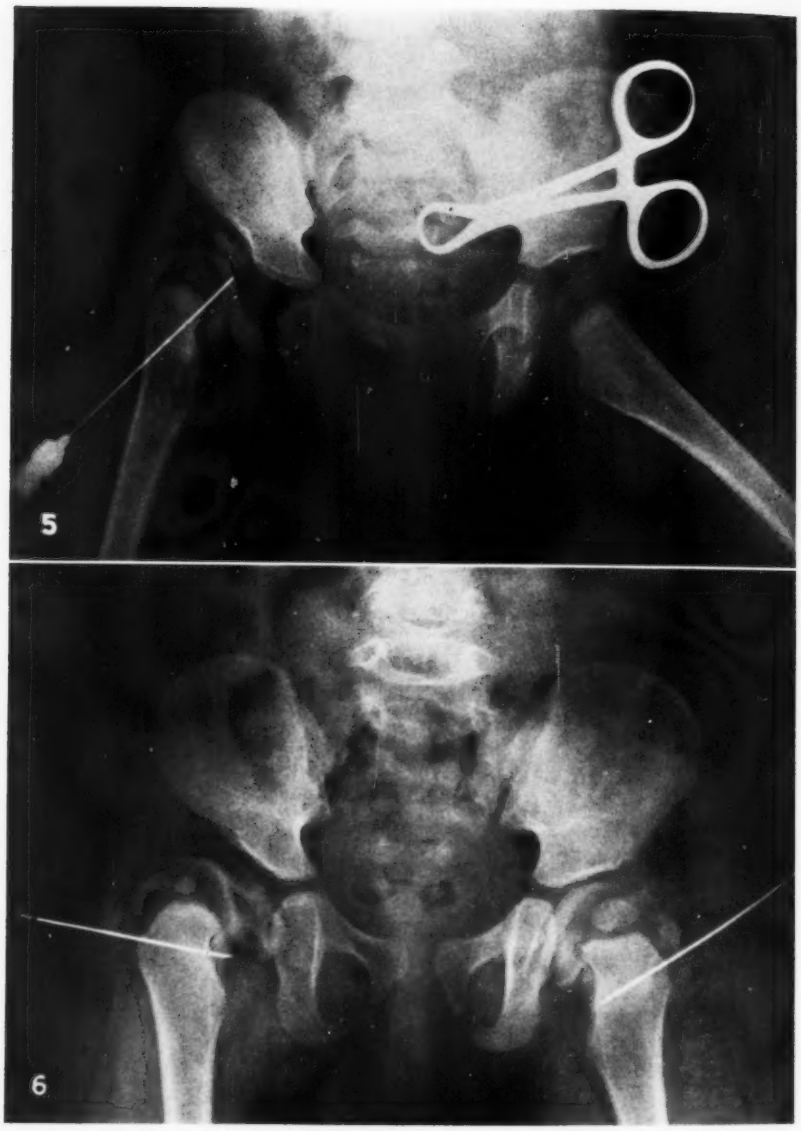

Fig. 5. Shallow acetabulum and acorn-shaped femoral head on the right. Complete dislocation.

Fig. 6. Hour-glassing of the capsule on the right side and a somewhat flattened femoral head. Widened hip joint space and well formed femoral head on the left.

tum teres, the position of the limbus, and the detritus in the acetabulum, as well as the hour-glassing of the capsule, probably would have presented formidable hazards for a closed reduction procedure. It has been found in hips presenting the type of configuration noted here that the capsule is frequently thickened to an abnormal degree, at times reaching a centimeter in thickness.

Figure 4 is a bilateral arthrogram providing a rather classical demonstration of what Leveuf postulated concerning the luxated and subluxated hip. On the right side,

there is a dysplasia of the combined type involving the femoral head and the acetabulum, and this is associated with a complete lateral and superior dislocation. In addition, the head of the right femur is acorn-shaped, there is hour-glassing of the capsule, the ligamentum teres is thickened, and the inlet for the acetabulum is markedly narrowed as a result of projection of the hypertrophied limbus downward and inward. There is also suggested fixation of the capsule to the side of the right ilium. The distortion of the right femoral neck is not commented upon at this time, as this does not primarily concern arthrography but can be evaluated from the plain horizontal-lateral views.

Coincidentally, on the left side it is noted that the limbus projects outward and slightly upward. However, the hip joint space is definitely widened—the so-called subluxated hip of Leveuf. It is felt that this type of hip lends itself admirably to closed reduction. The orbicular ligament on the left indents the capsule prominently, but there is no evidence of hypertrophy of the ligamentum teres in this arthrogram.

The arthrogram reproduced in Figure 5 shows a considerable amount of detritus in a shallow acetabulum on the patient's right, and an acorn-shaped right femoral head. The complete dislocation was apparent from the plain films, but the laxity and reduplication of the capsule were not previously apparent.

In Figure 6, the situation is similar to that in Figure 4, with hour-glassing of the capsule on the right side, moderate detritus in the base of the right acetabulum, hypertrophied ligamentum teres, and a somewhat flattened right femoral head. On the left side the hip joint space is widened and there is a rather well formed uncalcified femoral head.

SUMMARY

Arthrography has been performed at the St. Charles Hospital (Brooklyn, N. Y.) in 49 cases representing a rather wide selection of patients in the age group from two weeks to thirteen years. Renografin is the medium of choice. This is not a routine procedure but is limited to specifically selected cases, in which it has been found to be of help to the clinician in making a decision between closed and open reduction. The method has been without mortality or morbidity and there have been no local reactions to the procedure.

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SUMMARIO IN INTERLINGUA

Arthrographia del Coxa in Juveniles

Al Hospital St. Charles (Brooklyn, N. Y.), arthrographia del coxa esseva effectuate in 49 casos representante un large selection de patientes de etates de inter duo septimanas e dece-tres annos. Il se tracta hic non de un mesura routinari sed de un procedimento restringite a casos specificamente seligite. In tales illo se ha provate de valor como adjuta al clinico in decider se inter reduction claudite e reduction aperte. Le methodo ha remanite sin mortalitate o morbiditate.

Combined Intraventricular and Intracerebral Hydatid Cysts[1]

Report of a Case[1]

VINCENZO VALENTINO, M.D.

OF THE TOTAL number of hydatid cysts, probably about 2 per cent occur in the brain. Echinococcal infestation, as is well known, results from ingestion of ova of *Echinococcus granulosus* (*Taenia echinococcus*) in food or water, or directly from hands contaminated by contact with infested dogs. From the digestive tract the embryo enters the blood stream. Before reaching the brain, or any other organ of the body, it must pass through the capillary filter of the liver and lungs, which accounts for the coincidental occurrence of cysts in the central nervous system and in the liver or lungs.

Fig. 1. Hydatid cyst in the right lung (laminagram).

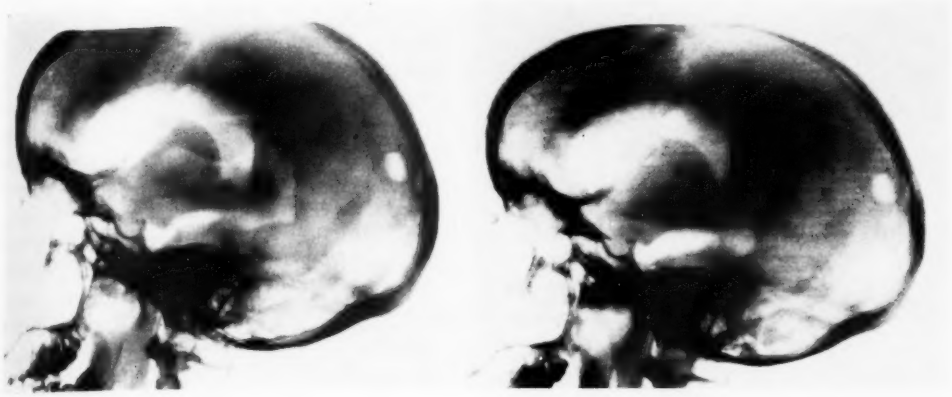
Opinions differ as to the incidence of the combined lesions. According to Dew (2), some 80 per cent of cerebral hydatid cysts occur in association with cysts in the liver. On the other hand, Araña and San Julián (1) in a series of 13 intracranial cysts found no instance of liver involvement and only 2 cases with associated pulmonary disease.

Fig. 2. Left carotid arteriogram, lateral view (the contrast medium has been injected into the common carotid artery). The last part of the carotid siphon as well as a portion of the anterior cerebral artery are moderately depressed. The pericallosal artery behind the genu of the corpus callosum bends upward, taking an exceptionally straight course.

Of interest in this connection is a case reported by Schroeder (4). His patient, a child with hydatid cysts in the lung and peritoneum, showed signs of an expanding intracranial lesion. This proved, however, to be not an hydatid cyst but a glioma of the cerebellar vermis. It thus appears that neither the presence nor absence of echinococcosis elsewhere can be accepted as conclusive evidence for or against a preoperative diagnosis of localization in the brain.

Intracranial echinococcosis occurs most frequently in the temporal and parieto-

[1] From the Neurosurgical Department (Director: Prof. Francesco Castellano) of the United Hospitals Naples, Italy. Accepted for publication in August 1958.



occipital regions in the form of a single cyst; multiple intracranial localizations are rarely encountered. The cyst commonly attains a large size, about 5 cm. or more in diameter, before coming to the attention of the neurosurgeon. This is due to the softness of the cerebral substance, which is easily displaced by the growing, non-infiltrating mass. It is of interest that, unlike other parasitic diseases, as for example cysticercosis, hydatid cysts in the ventricular cavities of the brain are almost unknown. As far as we have been able to learn, the only such case in the literature is that of Ruggiardo (3), who in 1902 reported perforation of the ventricle by an intracerebral cyst. The occurrence of associated but independent cerebral and ventricular localizations is therefore of more than usual interest.

CASE REPORT

A. E., a girl of 17 years, known to have an hydatid cyst in the right lung (Fig. 1), was admitted to the hospital complaining of severe headache, vomiting, and diminishing visual acuity for the preceding month. On clinical examination the patient appeared disoriented, but no localizing neurological signs could be elicited. Encephalography was attempted, but after the introduction of a few cubic centimeters of gas the patient collapsed and the procedure was abandoned. A frontal roentgenogram was obtained, however, showing small amounts of air within the right lateral ventricle, which was displaced toward the right side. An attempt at angiography of the left internal carotid artery was then made, but the patient was not co-operative, and only a lateral view was obtained (Fig. 2). Obviously this was not considered valuable for a definite diagnosis. Since the condition of the patient grew rapidly worse, two burr holes were made in the occipital regions and gas was injected into the lateral ventricles. Ventriculograms obtained after this procedure showed definite evidence of at least two cystic space-occupying lesions in the left lateral ventricle and one or two others outside the ventricle, exerting pressure on its roof (Fig. 3).

Fig. 3. Multiple intraventricular and extraventricular space-occupying lesions of cystic type are seen markedly deforming the enlarged left lateral ventricle.

At operation (Dr. F. Castellano), five cysts were removed from the left cerebral hemisphere, two of which were within the lateral ventricle (Fig. 4). The postoperative course was uneventful, and the patient left the hospital apparently recovered from the brain lesions.

Fig. 4. The surgical specimen.

COMMENT

The preoperative diagnosis of intracranial hydatid cyst is of high value, as surgical approach to the lesion without a knowledge of its real nature could lead to rupture of the cyst and to wide dispersion of hydatids. In view, however, of the resemblance of the symptoms to those of brain tumor, misdiagnosis seems to be unavoidable unless cysts are known to be present in the lungs or liver. Even under these circumstances presumptive diagnosis of the intracranial lesion rests essentially upon a neuroradiologic basis. This leaves little room for doubt. According to Araña and San Julián, angiography is the most reliable method of establishing the diagnosis of avascular space-occupying lesions of cystic type; when echinococcus is suspected, this is the neuroradiological procedure of choice, rather than ventriculography, which is dangerous. In this connection, the above mentioned authors reported a case of hydatid cyst mistaken for a posterior fossa tumor and punctured during ventriculography.

In principle we agree with Araña and San Julián. We would like, however, to emphasize the definite usefulness of air studies for the diagnosis of small cysts and those in localizations in which angiography is known to be of little help, *i.e.*, intraventricular cysts. In the case reported above, the lateral arteriogram did not provide detailed information as to the nature, site, and multiplicity of the lesions. The question arises whether a frontal view would have been of greater value in this respect. On the other hand, accidental puncture of the cyst during direct injection of gas within the ventricles must be considered as a possibility. In our opinion, this is not sufficient to constitute a serious contraindication to ventriculography, especially if the lesion is located elsewhere than in an occipital lobe. At most, in cases of suspected echinococcosis one could take the precaution of injecting air only in the ventricle opposite the side of the possible lesion.

SUMMARY

A case is reported in which multiple cerebral hydatid cysts occurred in a patient known also to have hydatid disease in the right lung. Two of the cysts were within the lateral ventricle and the remainder were situated in the left cerebral hemisphere outside the ventricle. This association of intracerebral and intraventricular hydatid cysts is unique.

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SUMMARIO IN INTERLINGUA

Combinate Cystes Hydatidic Intraventricular e Intracerebral: Reporto de Un Caso

Es reportate un caso de associate sed independente cystes hydatidic in le ventriculo sinistro-lateral e le substantia cerebral extraventricular. Un sol caso de localisation intraventricular de morbo hydatidic esseva trovabile in le litteratura (Ruggiardo, citate per Arana-Iniguez e San Julian: J. Neurosurg. 12:323, 1955). In ille caso un cyste intracerebral habeva producite un perforation a in le ventriculo.

Penumbra Measurements of Supervoltage and Cobalt-60 Machines by a Photographic Method[1]

LEONARD STANTON, M.S.[2]

In conventional 250-kv x-ray therapy, the treatment field is readily delineated. Even when significant penumbra is produced by the cone system, lead rubber may normally be used to shield healthy structures surrounding the tumor. Unfortunately, such a simple and effective procedure is impossible with cobalt 60. Thick shields are required (about 3.5 cm. lead for 10 per cent transmission), and even these must be positioned at least 15 to 20 cm. from the patient to avoid loss of the skin-sparing effect by electron contamination (1). Cobalt-60 sources now in use range up to 2.54 cm. diameter and higher, so that penumbras of several centimeters are not uncommon, as compared with a few millimeters in 250-kv therapy.

The clinical importance of large penumbras is illustrated in Figures 1 to 3. For Figure 1, a film was exposed to a 5 × 10-cm. beam, and the resultant density was measured. There is a marked overlapping of the field; also, the 90 per cent location is 1.0 cm. in on each side, so that the 90 to 100 per cent intensity area is only 3 × 8 cm., not 5 × 10 cm. In Figure 2, a well defined maxillary antrum portal is shown (supervoltage; 80 cm. T.S.D.) Here the coincidence of the beam edges with the desired portal outline is noteworthy. By contrast, Figure 3A shows the same field

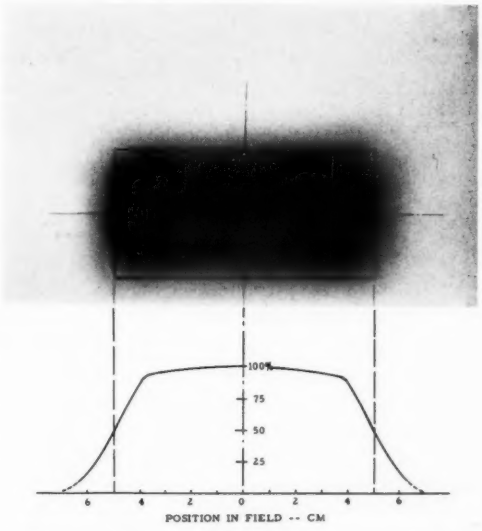

Fig. 1. Radiograph of a 5 × 10-cm. cobalt-60 treatment field. Lower graph shows variation of intensity across field.

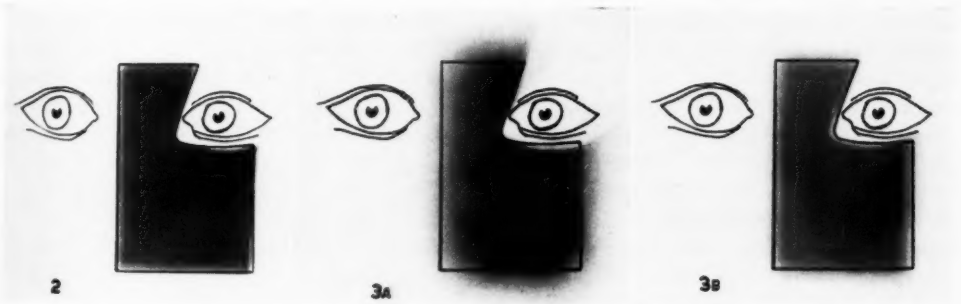

Fig. 2. Maxillary antrum portal: small penumbra.
Fig. 3. Maxillary antrum portal. A. Large penumbra. B. Moderate penumbra.

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[1] From the American Oncologic Hospital and Lankenau Hospital, Philadelphia, Penna. Presented at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16–21, 1958.

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TABLE I: PERTINENT DATA FOR TWO SUPERVOLTAGE AND FOUR COBALT-60 UNITS STUDIED

Type of Unit	Location[1]	Source, Size	Collimator Design
Supervoltage[2]	American Oncologic Hospital	4–5 mm. diam.	2 inch lead blocks, one set[3] mounted above other set
Supervoltage[4]	University of Pennsylvania Hospital	4–5 mm. diam.	3 inch lead blocks, one set[3] mounted above other set
Picker C-3000 (K)[6]	Jefferson Hospital	1.0 inch diam.	Johns[7]
Theratron (K)	Lankenau Hospital	2.0 cm. diam.	Coplanar 2 inch thick tungsten blocks[5]
Picker C-1000 (H)	Reading Hospital	Cloverleaf	Johns (modified)
Keleket Rotaray (H)	Albert Einstein Medical Center, Northern Division	1.0 inch diam.	Lead blocks on spherical surface[7]

[1] All in Philadelphia, except Reading Hospital, Reading, Penna.
[2] Experimental unit, made in 1948, at High Voltage Research Laboratory, Massachusetts Institute of Technology, Cambridge, Mass.
[3] Block faces angled 4° to minimize penumbra.
[4] Commercial unit Model AM, made by High Voltage Engineering Corporation, Burlington, Mass., installed in February 1958.
[5] Block faces parallel to each other and to central ray.
[6] K means kilocurie or high-intensity cobalt-60 unit; H, hectocurie or low-intensity unit.
[7] Useful beam always parallel to collimator surface, for any size field, so it does not strike collimator material at glancing angle.

treated with a beam of large penumbra. In Figure 3B, this was greatly reduced by irradiating at 50 cm. instead of 80 cm. This effect is most significant in treating small fields, particularly about the head and neck, though it may be important for larger fields also.

Penumbra has been discussed frequently in the literature (2–9). Several papers indicate a greater spreading of isodose lines with cobalt than with conventional x-ray machines (4, 5, 7, 8, 9), but to the writer's knowledge only one reports direct measurements of penumbra. Tsien and Robbins (4) determined the position in the beam of the 90, 80, 50, 20, and 10 per cent of central ray intensity, for a Picker C-1000 unit, at 50 cm. S.S.D., employing a cobalt-60 source 2 cm. in diameter.

In view of the clinical importance of this information for each source size, collimating system, and treatment distance used, a study was undertaken to provide more comprehensive data on several representative machines (see Table I for descriptive details). In practice, wide variations are possible in factors affecting penumbra—even for a given unit. For this reason, the method employed to measure penumbras is described in some detail; also, a discussion of penumbral formation is presented, which permits a simple calculation of penumbra for a given situation. These data give a fairly complete picture of the intensity distribution across the treatment beam when combined with the fact that the light beam edge corresponds to the 50 per cent location in all four cobalt units tested.[3]

Penumbra data are given in Figure 9 and Tables V to X. The tables show the location in the beam of the 90 to 10 per cent of central ray intensities, where the 50 per cent line is taken as zero. Intensities greater than 50 per cent occur closer to the central ray; their positions are indicated as minus distances, to distinguish them from those of intensities less than 50 per cent, which are further from the central ray.

METHOD OF MEASUREMENT

It is well known that ionization chambers permit the most accurate radiation dosage measurements. Technical difficulties, however, make their use difficult in this application. Since penumbra widths may be less than 1.0 cm., it is necessary to use an ionization chamber 1.5 mm. or less in width; also, positioning must be accurate to ± 0.2 mm. While this is technologically possible, it involves far more difficult problems than positioning an 8×10-in. film along a millimeter scale. Since the re-

[3] Optical alignment must be checked by film regularly, as light beam systems now in use tend to get out of adjustment. Also, they can be set accurately at only one S.S.D., since the optical and radiologic penumbras are not identical.

quired accuracy was attainable with a film method, this was chosen as the most practical solution of the problem.

An error in penumbral position of ± 0.5 mm. is taken as clinically acceptable. While this does not represent extreme precision, it nevertheless requires that certain factors be carefully considered. Among these are the following: (*a*) fogging factors, (*b*) film response and exposure and, (*c*) densitometry.

In addition to the roentgen exposure, the density of a film is known to be affected by fogging action of vapors, other radiation exposure, and developing and fixing. For this reason, only relative rather than absolute measurements are usually practical. In the present application, any generalized uniform film density is simply subtracted from the measured value. Since relative corrected densities are employed, only linearity of response affects the result. By the use of standard good processing technics, quite consistent results have been obtained.

Hine (11) has discussed film response to radiation in some detail. Two distinct questions are involved: (*a*) How does the film respond to the same roentgen doses of hard and soft radiation? (*b*) For a given quality of radiation, does the density increase linearly with dosage?

For x-rays generated at 250 kv and lower, all films are dependent on beam photon energy. In the cobalt-60 and supervoltage range, however, the response is substantially independent of kev. This is fortunate, because Compton-scattered photons are softer than those of the primary beam, and both strike the film.

Only certain films respond linearly with radiation dosage. Granke *et al.* (12) have used Type A Kodak Industrial film; this has a linear response up to densities of nearly 3.0 (11). In the present measurements, Ansco non-screen films were used for preliminary work. They were of the type individually packaged in paper holders. The data reported here, however, were obtained with Kodak type M industrial film. This is similar to type A in linearity but is

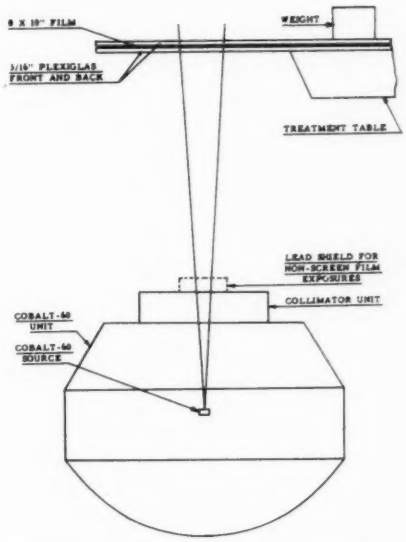

Fig. 4. Set-up for exposure of films in penumbra measurements.

of considerably lower speed, which is helpful in obtaining practical exposure times. The M film was substituted for the non-screen film and the envelope resealed. Care in handling was necessary to avoid pressure artefacts. During exposure, the film was placed perpendicular to the central ray, with 3/16-in. Plexiglas sheets held tightly front and back to assure electron equilibrium. The physical set-up is shown in Figure 4.

Non-screen film is about ten times as sensitive to cobalt-60 rays as type M industrial film. For usable exposures, times are of the order of one and ten seconds, respectively. Since a shutter takes a finite time to open and close, there is danger of an inhomogeneous exposure with non-screen film (*i.e.*, one side darker than the other). To reduce this effect, a 1 1/4-in. lead absorber was used close to the source to reduce the intensity about eight times. It was of laminated construction, consisting of twenty 1/16-in. lead sheets taped together (solid castings are often inhomogeneous).

Figure 5 shows linearity curves of Ansco non-screen and Kodak type M industrial films. Individual films were carefully exposed to 100 kvcp, 15 ma, Thoraeus II

TABLE II: COMPARISON OF PENUMBRA DATA OBTAINED USING INDUSTRIAL (I) FILM VS. NON-SCREEN (NS) FILM CORRECTED FOR NON-LINEAR RESPONSE

Per Cent of Central Ray Intensity	Position in Penumbra (mm.) for S.S.D.					
	50 cm.		70 cm.		90 cm.	
	I	NS	I	NS	I	NS
90	−5.2	−5.0	−9.5	−9.1	−13.2	−13.1
80	−3.5	−3.5	−6.6	−6.4	−9.5	−9.2
70	−2.3	−2.4	−4.2	−4.1	−6.1	−6.2
60	−1.1	−1.2	−2.2	−2.0	−2.9	−3.2
50	0	0	0	0	0	0
40	1.2	1.2	2.1	2.1	3.0	3.4
30	2.5	2.6	4.3	4.5	6.4	7.2
20	4.1	4.4	6.9	7.2	10.5	11.4
10	6.1	7.0	10.2	11.0	15.0	16.5

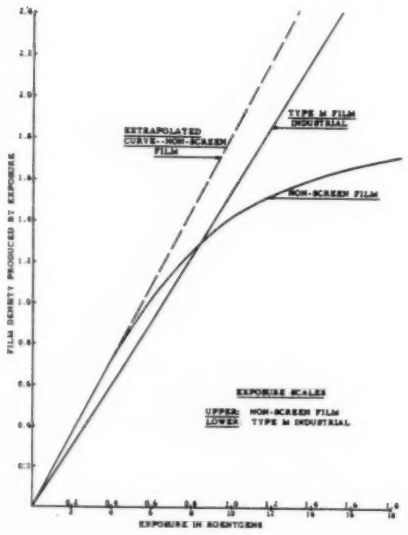

Fig. 5. Film response curves, showing density *vs.* exposure dose in roentgens for Kodak type M industrial and Ansco non-screen film. Plotted on linear scale.

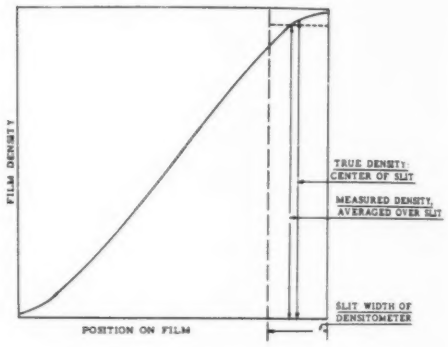

Fig. 6. Nature of density sampling error.

x-rays at 150 cm. T.S.D., in steps of three and thirty seconds. Transmission effects were minimized with 1/4-in. lead. Density data obtained from these curves were then correlated with cobalt-60 measurements to obtain Figure 5. While the absolute roentgen dosages are only approximately correct, the curve linearity is in good agreement with the manufacturer's data, and is quite reliable.

There is a slight bend in the type M film curve at 0.6 density; above this, it is linear to 3.0. For this reason, these films were pre-exposed to a uniform density of 0.6, using the 100 kvcp beam mentioned above. Tests showed this pre-exposure to be uniform on any given film to ±0.01 density. Non-screen film was not pre-exposed, as its linearity is increasingly poor when density is increased.

Industrial film is obviously preferable to non-screen for this work. It is possible, however, to use non-screen film and correct measured densities with the aid of the dotted curve in Figure 5. Table II compares results obtained with the two films, for the Theratron unit. Data are substantially the same except for the 10 and 20 per cent intensity figures (at the marginal edge of the beam).

DENSITOMETRY

A "Photovolt" transmission photomultiplier type densitometer was employed for film density measurements. The optical system was refocused and realigned to assure proper optical stability. The round light opening (4 mm. in diameter) was then

masked down with black tape to a width of 1.5 mm.; a smaller unit would be preferable, but 1.5 mm. was needed to obtain sufficient meter deflection. The instrument itself was quite consistent and stable. Readings were repeatable to 0.03 for densities up to 3.5, generally to 0.01 or better. Judging from the design and performance of the unit, instrument linearity was more than enough to meet the accuracy requirements.

Since the penumbras may be less than 10 mm. wide, the 1.5-mm. sampling slit width can introduce a significant averaging error. Figure 6 shows how the measured density differs from that at the center of the slit. This tends to make the measured curve less angular than the true curve, giving higher figures for 10 to 90 per cent intensity locations, but no significant effect in between. A second theoretical type of sampling error is due to the logarithmic inference by the densitometer of density from a transmission measurement (transmission equals $10^{-\text{density}}$) (see Fig. 7). The density read on the scale is somewhat lower than the true density at the slit center, even for a straight portion of the penumbral curve. An analysis of this effect has been made but is beyond the scope of this paper. Calculation shows that the error never approaches 1 per cent of the density value for the experimental conditions employed here, so it is neglected.

The experimental error in density measurement is believed to influence the penumbra measurements negligibly.

NATURE OF PENUMBRA FORMATION

A simplified representation of penumbra formation has been previously described (2, 3), but it does not explain the experimental curve. Among the causes for this inadequacy are the following three effects.

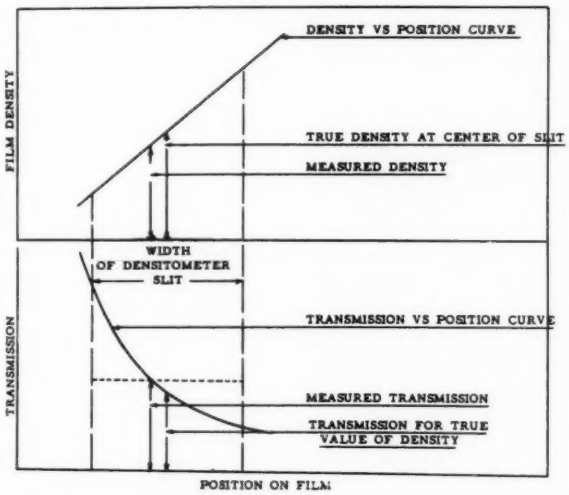

Fig. 7. Nature of error induced by averaging transmission value in densitometry.

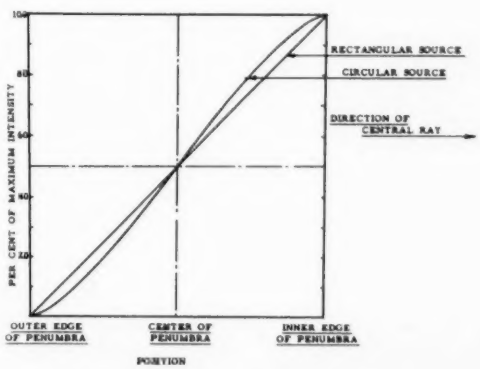

Fig. 8. Theoretical variation of intensity in penumbral region: rectangular *vs.* round source.

TABLE III: SAMPLE PENUMBRA CALCULATION*

Per Cent of Central Ray Intensity	"b"† for 1 cm. diam. Source	"b" for 2 cm. diam. Source	Geometric Factor- d_2/d_1	Calculated Penumbra Position	Measured Penumbra Position
	mm.	mm.		mm.	mm.
90	−3.44	−6.87	1.259	−8.65	−9.5
80	−2.46	−4.92	1.259	−6.19	−6.55
70	−1.59	−3.19	1.259	−4.01	−4.2
60	−0.79	−1.58	1.259	−1.98	−2.2
50	0	0	1.259	0	0
40	0.79	1.58	1.259	1.98	2.1
30	1.59	3.19	1.259	4.01	4.3
20	2.46	4.92	1.259	6.19	6.85
10	3.44	6.87	1.259	8.65	10.2

* These data apply to a cobalt teletherapy unit for which (1) source size is 2.0 cm. diameter; (2) distal collimator surface is located 31 cm. from source (d_1); (3) S.S.D. is 70 cm. so that collimator-skin distance is 70—31 or 39 cm. (d_2).

† "b" is numerically equal to the theoretical penumbral location when d_1 and d_2 are equal.

TABLE IV: RATIO OF MEASURED TO CALCULATED PENUMBRAL POSITIONS

Per Cent of Central Ray Intensity	Picker C-3000	Theratron	Picker C-1000	Keleket Rotaray
90	1.10	1.06	1.32	1.31
80	1.10	1.04	1.11	1.26
70	1.11	1.025	1.03	1.21
60	1.10	1.03	1.04	1.17
50	...	...	...	...
40	1.16	1.03	1.03	1.15
30	1.14	1.06	1.08	1.18
20	1.14	1.12	1.14	1.27
10	1.36	1.16	1.28	1.62
Av.—20 to 80 per cent	1.14	1.05	1.07	1.21
SSD, cm.	100 to 120	70 to 90	50 to 55	60
Collimator-to-skin distance, cm.	40 to 60	39 to 59	22 to 27	30

TABLE V. INTENSITY VARIATION IN PENUMBRAL REGION FOR VARIOUS T.S.D. VALUES: SUPERVOLTAGE UNIT AT AMERICAN ONCOLOGIC HOSPITAL

Per Cent of Central Ray Intensity	Position in Penumbra for T.S.D. of: 55 cm.	70 cm.	90 cm.
	mm.	mm.	mm.
90	−1.5	−2.4	−3.4
80	−1.0	−1.5	−1.8
70	−0.6	−0.9	−1.1
60	−0.3	−0.4	−0.6
50	0	0	0
40	0.4	0.6	0.7
30	1.0	1.3	1.4
20	1.7	2.2	2.4
10	3.1	4.5	4.6

First, the radiation source in cobalt and supervoltage machines is circular rather than rectangular. This causes the source edges to contribute relatively little intensity as compared with the central part. A rectangular source tends to produce penumbral intensities varying linearly with position (Fig. 8). However, the penumbral intensity of a circular source varies more rapidly near the center, more slowly near the edges. This "S"-shaped curve tends to reduce lateral displacements of the 90, 80, and 70 per cent intensity locations by about a fifth. This means that the most clinically significant penumbra is reduced 15 to 20 per cent by the use of a circular rather than rectangular source—an unexpected benefit.

A second effect, however, tends to increase penumbra. This is the forward scatter from the collimator walls. This effect is greatest when the collimator is closer than 30 cm. to the skin; for this reason, penumbra is not substantially benefited in hectocurie machines by extremely close treatment distances, because the benefit from geometric reduction tends to be cancelled by increased scatter effect. Table IX shows, for example, that the reduction in penumbra in operating a Picker C-1000

TABLE VI: INTENSITY VARIATION IN PENUMBRAL REGION FOR VARIOUS T.S.D. VALUES: SUPERVOLTAGE UNIT AT UNIVERSITY OF PENNSYLVANIA HOSPITAL

Per Cent of Central Ray Intensity	Position in Penumbra for T.S.D. of: 55 cm. A	55 cm. B	70 cm. A	70 cm. B	90 cm. A	90 cm. B
	mm.	mm.	mm.	mm.	mm.	mm.
90	−2.5	−3.3	−2.8	−4.3	−3.5	−4.4
80	−1.7	−2.2	−2.0	−2.9	−2.45	−3.0
70	−1.1	−1.4	−1.3	−1.8	−1.55	−1.9
60	−0.5	−0.65	−0.6	−0.9	−0.75	−1.0
50	0	0	0	0	0	0
40	0.6	0.7	0.65	0.9	0.75	1.05
30	1.25	1.5	1.35	1.9	1.6	2.1
20	2.2	2.8	2.3	3.2	2.6	3.5
10	3.6	5.5	3.7	5.6	4.1	5.7

unit at 40 cm. S.S.D. instead of 50 cm. is relatively slight, even though an almost 50 per cent reduction is expected on the basis of geometric considerations alone.

A third effect, mentioned previously (6), results from significant transmission of the beam through the collimator by radiation striking it obliquely. It appears that this effect has been minimized by design in modern cobalt units for primary beams. (In the Theratron, tungsten is used as collimator, and therefore little transmission occurs. In the other three units measured, the useful beam never strikes the absorber obliquely, because of ingenious collimator design.) However, in all cases the scattered rays emerging strike obliquely, and have some effect.

Due to the relatively large source in cobalt machines, the first effect is most important in these, especially at greater distances. In the Van de Graaff units, focal spot areas are of the order of 4 to 5 mm. diameter, so that geometric aspects of penumbral formation are less important than in cobalt machines, and the other effects become relatively more significant. This is shown by the relatively small reduction in penumbra when treatment distance is reduced from 90 to 70 cm. (Table VI).

TABLE VII: INTENSITY VARIATION IN PENUMBRAL REGION FOR VARIOUS S.S.D. VALUES: PICKER C-3000 COBALT-60 UNIT AT JEFFERSON HOSPITAL

Per Cent of Central Ray Intensity	Position in Penumbra for S.S.D. of: 80 cm.	100 cm.	120 cm.
	mm.	mm.	mm.
90	−3.9	−6.4	−9.5
80	−2.6	−4.7	−6.8
70	−1.7	−3.1	−4.4
60	−0.85	−1.5	−2.2
50	0	0	0
40	0.9	1.5	2.4
30	1.9	3.0	4.6
20	3.0	4.8	7.2
10	5.3	8.1	11.6

Calculations have been made of penumbral positions for all of the cobalt units, using Figure 8 as a basis. Table III indicates the steps in such a calculation, for a Theratron unit; Table IV shows the ratio of measured to calculated values for four cobalt units. This calculation ignores collimator scatter and scatter transmission effects. Since these are relatively large in

TABLE VIII: INTENSITY VARIATIONS IN PENUMBRAL REGION FOR VARIOUS S.S.D. VALUES: THERATRON COBALT-60 UNIT AT LANKENAU HOSPITAL

Per Cent of Central Ray Intensity	Position in Penumbra for S.S.D. of: 50 cm.	60 cm.	70 cm.	80 cm.	90 cm.	100 cm.
	mm.	mm.	mm.	mm.	mm.	mm.
90	−5.2	−7.3	−9.5	−11.3	−13.2	−15.0
80	−3.5	−5.0	−6.6	−8.0	−9.5	−11.0
70	−2.3	−3.2	−4.2	−5.2	−6.1	−7.2
60	−1.1	−1.6	−2.2	−2.6	−2.9	−3.2
50	0	0	0	0	0	0
40	1.2	1.6	2.1	2.5	3.0	3.4
30	2.5	3.4	4.3	5.3	6.4	7.4
20	4.1	5.5	6.9	8.5	10.4	12.5
10	6.1	8.1	10.2	12.4	15.0	17.6

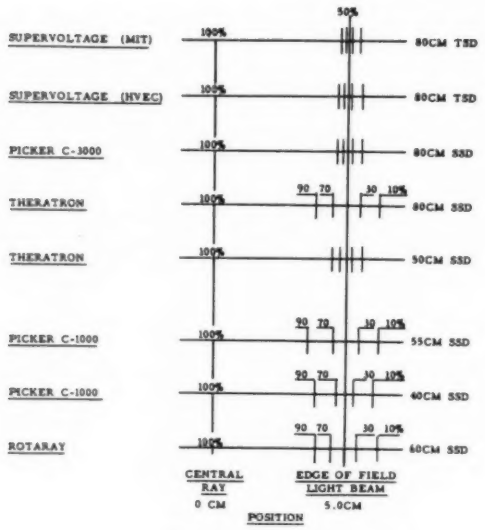

Fig. 9. Location of 100, 90, 70, 50, 30, and 10 per cent of central ray intensities in a 10-cm. field, at various useful treatment distances.

supervoltage units, agreement is found only for 60 to 90 per cent intensities, becoming poor below 50 per cent; fortunately, penumbral values are very small in Van de Graaff units (Tables V and VI), and it is not important clinically to know them with precision.

Table IV shows surprisingly close agreement between theory and experiment. This encourages the calculation of penumbral figures of cobalt units, where new technics and equipment exist, with the use of this table to obtain suitable correction factors.

EXPERIMENTAL RESULTS

Figure 9 is a visual presentation of penumbral data for the six units measured, at a few useful treatment distances. A field 10 cm. wide is assumed in each case. Positions of 90, 70, 50, 30, and 10 per cent of central ray intensity are indicated by vertical lines, labeled for larger penumbras. More complete data are given in Tables V to X, with information for a larger variety of treatment distances.

These measurements apply primarily to fields of 7 to 12 cm. They represent the

TABLE IX: INTENSITY IN PENUMBRAL REGION FOR VARIOUS S.S.D. VALUES: PICKER C-1000 COBALT-60 UNIT AT READING HOSPITAL

Per Cent of Central Ray Intensity	Position in Penumbra for S.S.D. of: 40 cm.	50 cm.	55 cm.
	mm.	mm.	mm.
90	−11.2	−9.9	−14.1
80	−5.5	−6.4	−8.0
70	−3.3	−4.0	−4.6
60	−1.6	−1.9	−2.4
50	0	0	0
40	1.6	1.9	2.4
30	3.4	4.0	5.0
20	5.7	6.5	8.1
10	10.7	10.5	12.7

TABLE X: INTENSITY VARIATION IN PENUMBRAL REGION FOR VARIOUS S.S.D. VALUES: KELEKET BARNES "ROTARAY" COBALT-60 UNIT AT ALBERT EINSTEIN MEDICAL CENTER, NORTHERN DIVISION

Per Cent of Maximum Intensity	Position in Penumbra for S.S.D. of 60 cm.
	mm.
90	−10.9
80	−7.7
70	−5.0
60	−2.4
50	0
40	2.4
30	4.9
20	7.7
10	12.9

majority of cases for which this type of information is of interest. With larger fields, the penumbra tends to be slightly larger. However, the optical system then defines the 50 per cent line with less accuracy than with smaller fields, so that there is little point in presenting special penumbra data. Improvement in optical field-defining systems appears to be a desirable project for designers of cobalt units.

DISCUSSION

It is evident that penumbra depends on many factors other than the cobalt shield design. Source size is an important consideration. However, with proper collimator design, a large source may be used with negligible penumbra (Table VII). On the other hand, smaller (hectocurie) units exhibit the largest penumbras at present, due basically to the necessity for short treatment distances resulting from use of weaker sources of large diameter. High-intensity 1.0-cm.-diameter sources are ap-

parently in prospect. These would reduce penumbra values by a factor of about two, to fairly good levels. It should be emphasized that smaller sources improve only the geometric aspects of penumbra formation, and that full improvement will be noted only for significant collimator-skin distances, for which scatter effects are not excessive.

The Theratron unit was tested without the use of available collimator extensions. While penumbra is substantial at 80 cm. S.S.D., this is reduced substantially at 50 cm., which is therefore used in treating head and neck lesions. The available extensions would make this unit reasonably comparable to the Picker C-3000 unit in penumbra, but the problem then arises of collision with the treatment table in rotation therapy. Use of arc rotation may therefore offer some advantages in this unit.

The Van de Graaff supervoltage units exhibited the smallest penumbras. Values appear to be smaller than those previously reported by Wootton (5). This is apparently due to an excessive focal spot size in his unit (9 mm.), about double the values usually found, according to Trump's group at Massachusetts Institute of Technology (10). If we assume 4 to 5 mm. for the units tested, the calculated penumbral values are comparable with measured values.

SUMMARY

The clinical significance of penumbra in cobalt-60 therapy is demonstrated by films, and the need indicated for adequate intensity measurements in the penumbral region. A wide variety of conditions exist in practice which affect penumbra. As a result, it is impractical to measure every possible case individually. For this reason, a study has been made of penumbral formation, and a simple method is presented for calculating penumbra values to a useful degree of accuracy for any given treatment situation. This method is shown to apply to four types of cobalt-60 units, at a variety of treatment distances. Experimental penumbral values are given for six machines, at various distances. The practical significance of the observed results is discussed.

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(Por el summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Mesurationes de Penumbra de Machinas de Supervoltage e a Cobalt-60 per Medio de un Methodo Photographic

Es demonstrate le signification clinic de penumbra in therapia a cobalt-60 per medio de pelliculas radiographic. Es signalate le necessitate de obtener adequate mesurationes de intensitate in le region penumbral. A causa del facto que il existe in le practica un extense varietate de conditiones que affice le penumbra, il non es possibile mesurar omne genere de caso individualmente. Per consequente, le formation del penumbra esseva studiate, e un simple methodo photographic esseva disveloppate pro calcular le valores de penumbra con un grado acceptabile de accuratia pro omne situation therapeutic particular. Es constatate que iste methodo es applicabile a quatro typos de machina a cobalt-60, con un varietate de distantias.

Es includite tabulas que monstra valores penumbral experimental pro sex machinas therapeutic a differente distantias. Iste mesurationes vale primarimente pro campos de inter 7 e 12 centimetros de diametro le quales representa le majoritate del casos in que iste typo de information es de interesse.

Attenuation of Scattered Cesium-137 Gamma Rays[1]

F. S. FRANTZ, JR.,[2] and H. O. WYCKOFF

THE IMPORTANCE of having attenuation curves available of radiation scattered from objects in the useful beam, such as the walls of a radiation room or a patient, has already been pointed out (1). Each irradiated object becomes a source of secondary radiations which may be hazardous to personnel located in areas away from the direction of the useful beam. Only by knowing the attenuation curves of the secondary radiation in common protective materials, such as lead or concrete, can the most economical secondary protective barriers be designed to eliminate this hazard.

The data available on the attenuation of scattered gamma rays are of two types. For one a suitable phantom is used to duplicate the conditions under which a patient scatters radiation out of the useful beam (2, 3). The second type consists of measurements in which the radiation is scattered from a concrete wall or barrier (2). The scattered radiation may traverse a longer path within the phantom than in the wall and thus be more greatly attenuated, so that the dose rate at a given distance from the scatterer may be higher for the second type of measurement. For a given moderate-to-hard quality of useful beam radiation, however, the quality of scatter at a given angle should not be very different for the two cases.

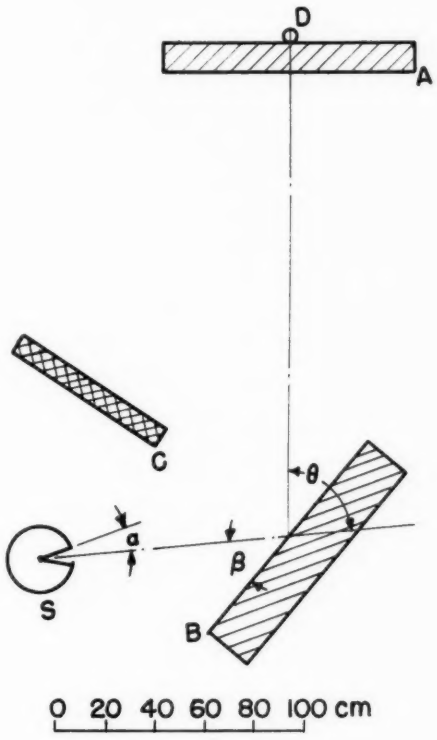

Fig. 1. Plan view of gamma scattering experiment. S. Source. B. Concrete barrier. A. Absorber. D. Detector. C. Shield. θ. Scattering angle. β. Barrier angle. α. Half-angle of primary beam.

Although interest in teletherapy sources has been directed chiefly to Co^{60} (2, 3) up to the present time, several other isotopes have characteristics which make them desirable for this purpose. Brucer (4) has pointed out the requirements of teletherapy source materials: source energy between 0.2 and 1.0 Mev to reduce the shielding requirements, high specific activity for small source size, long life, and availability. Cs^{137} with its thirty-year half-life and an energy of 0.66 Mev fulfills these requirements better than Co^{60} with a 5.2-year half-life and an energy of 1.2 Mev.

EXPERIMENTAL PROCEDURE

The geometry used in the experiment is shown in Figure 1. The 120-curie Cs^{137} source consisted of CsCl compressed into a stainless steel can with 1-mm. walls within a lead container approximately 11 in. in diameter, having a horizontal-axis conical opening of half angle 8.5°. The vertical scattering barrier, made up of concrete

[1] From the National Bureau of Standards. Work supported by the Atomic Energy Commission. Accepted for publication in September 1958.

[2] Now at Westinghouse Atomic Power Division.

blocks 6 × 8 × 12 in. laid up into a wall 40 in. wide, 42 in. high, and 8 in. thick, standing on a table 24 in. high, was located so that the source-to-barrier distance measured by the beam axis was 100 cm. and the barrier was at an angle, β, with respect to the axis of the incident gamma rays. The barrier was thick enough so that any increase in thickness would yield negligible increase in the scattered dose rate, as determined by an auxiliary experiment.

for each of the four detector positions.

The lead absorbers used were in the form of closed close-fitting cylinders concentric with the detectors. These were shown to yield the same results as flat sheets of lead.

The concrete absorbers were 4 × 8 × 12-in. blocks of concrete laid up into walls 36 in. across and 40 in. high, centered in front of the detector. Earlier work (5) in this laboratory indicates that concrete absorbers must be at least 36 in. in diameter

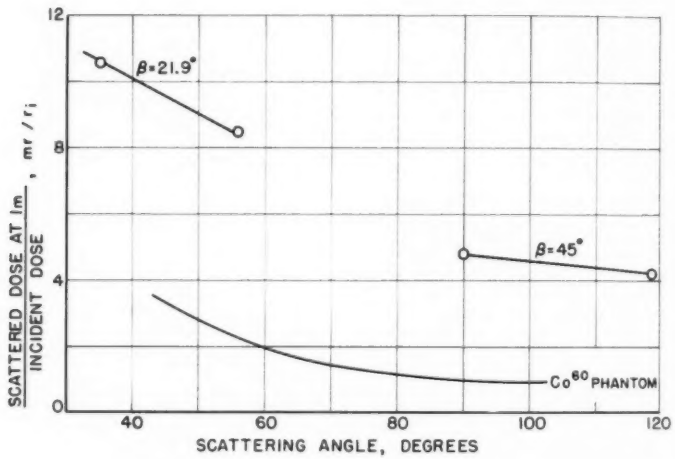

Fig. 2. Ratio of scattered dose at 1 meter from scatterer to incident dose *vs.* scattering angle. The circles indicate the data obtained for Cs^{137} gamma rays for two values of the scattering angle, β. For comparison purposes data obtained with approximately the same field size with Co^{60} and a phantom (2) are included.

The detectors used for the scattered-radiation measurements were condenser ionization chambers having maximum ranges of 10^{-2} and 10^{-3} r. Measurements were made at four different scattering angles, at the same height above the floor as the source, 200 cm. from the intersection of the central ray of the incident gamma beam with the scatterer. The scattering angle, θ, defined from the axis of the gamma ray beam, had values 35°, 56°, 90°, and 119°. For the first two of these, the angle β was 21.9°, and for the latter two, 45°. The detector was prevented from seeing the source container directly by means of a lead brick shielding wall, C, which was placed near the source holder and shifted

to achieve broad beam conditions; *i.e.*, that any increase in the lateral dimensions of the absorber will not result in an increase in the detector response, for a nearly parallel beam, although a diverging beam will not require so large an absorber. In any given 4-in. thickness of absorber, blocks were arranged in a pattern of best fit to reduce leakage at the joints. This pattern was maintained throughout the experiment. The average density of the concrete was found by weighing and measuring. The block thickness was then corrected to the equivalent thickness of concrete having a density of 147 lb./ft^3.

Background measurements were made by replacing the central 4-in. concrete

block, which was located immediately in front of the chamber, with 4 in. of lead. In addition, a 1/8-in. lead sheet was interposed between the detector and the concrete absorbing wall to absorb the secondary radiation emitted by the absorber.

DISCUSSION

The scattered radiation varies with angle both in intensity and in energy. Figure 2 shows the behavior of the scattered dose, multiplied by the square of the distance in meters from the scatterer, per unit incident dose, with scattering angle. As the scattering angle increases from 35 to 56°, the scattered dose per unit incident dose decreases, but is nearly the same at 90 and 117°. A similar curve obtained by Dixon *et al.* for cobalt-60 radiation showed somewhat lower values. Such a departure is expected, however, because more of the scattered radiation was attenuated in their phantom scatterer than in the concrete walls used here and because the relative amount of scattering is less from the higher-energy incident photons.

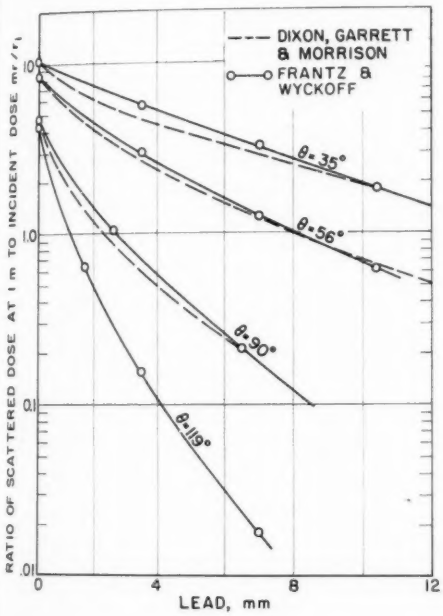

Fig. 3. Attenuation curves in lead for scattering angles of 35°, 56°, 90°, 119°. Also shown are theoretical curves based on Compton single scattering, attenuation curves from half-value layers obtained by Braestrup and Mooney using Co^{60}, and attenuation curves obtained by Dixon *et al.* using Co^{60}.

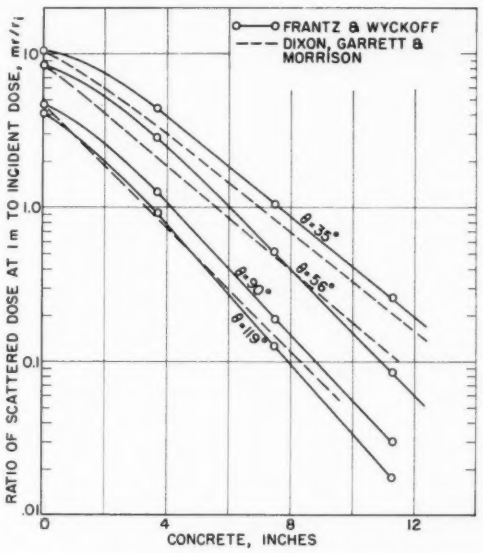

Fig. 4. Attenuation curves in concrete for scattering angles of 35°, 56°, 90°, 119°. Also shown are attenuation curves obtained by Dixon *et al.* using Co^{60}. The narrow beam data at 119° is compared with a theoretical curve based on Compton single scattering.

The attenuation curves of the scattered radiation in lead and concrete are given in Figures 3 and 4, respectively. The ordinate is the ratio of attenuated scattered dose at 1 meter from the scattering wall to the dose incident upon the wall measured in air, and is expressed in mr per incident roentgen. The change in the spectra of the scattered radiation, indicated by the changing slope, as the scattering angle increases, is quite apparent, especially in lead.

Although methods have been outlined for the computation of the amount of radiation scattered (6) and the broad beam attenuation of the scattered radiation, a rigorous treatment is difficult. The useful beam is contaminated with radiation scattered in the source and collimator, the finite size of the beam and detectors requires the consideration of a range of angles for each arrangement, and part of the radiation reaching the detector results from single scattering, and part from multiple scatter-

TABLE I: SCATTERING ANGLES FOR COBALT 60 AND CESIUM 137 RADIATION WHICH GIVE THE SAME ENERGY

Scattered Photon Energy (kev)	θ_{cs}	θ_{co}
533	35°	63°
417	56°	79°
285	90°	110°
224	119°	145°

ing. It is worthwhile, however, to try to compare the attenuations of the scattered beam obtained here with that obtained by Dixon *et al.* As a first approximation, it will be assumed that the useful beam contamination, the finite size of the detector, and the multiple scattering can be neglected. A scattering angle, θ_{co}, for cobalt-60 gamma rays may then be chosen so that the scattered photon energy, E_θ, will be the same as that for scattered cesium-137 gamma rays at an angle θ_{cs}. Values of θ may be obtained from the Compton relation

$$\frac{1}{E_\theta} = \frac{1}{E_0} + 2\,(1 - \cos\theta) \qquad (1)$$

where E_0 is 1.25 Mev for cobalt 60 and 0.66 Mev for cesium 137. Table I shows values of θ_{co} equivalent to the θ_{cs} obtained in the present experiment. One may then compare the attenuation of scattered photons at an angle θ_{cs} with that determined for θ_{co}. The dotted curves of Figures 3 and 4 have been obtained by interpolation from the plotted curves of Dixon *et al.* and normalization to the present data at zero thickness. The largest angle would have required an extrapolation not considered to be trustworthy. Dixon's results show a more rapid attenuation at small depths and a little less attenuation at greater depths. The reason for this is not clear but it may be due to some differences in geometry, particularly with respect to the relative location of absorber and detector. However, for the accuracy usually required for protection computation, the two studies may be considered to be in agreement.

CONCLUSIONS

1. The intensity of the scattered gamma radiation decreases approximately linearly as the scattering angle increases to 90° but thereafter decreases very little.

2. The attenuation of scattered cesium-137 gamma rays of an energy computed from the Comptom relation agrees with that obtained for scattered cobalt-60 gamma rays of the same energy with an accuracy usually required for protection work.

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SUMMARIO IN INTERLINGUA

Attenuation de Disperse Radios Gamma de Cesium-137

Curvas de attenuation a fasces large pro le radiation disperse de fontes teletherapeutic es necessari in elaborar barrieras de protection radiational secundari. Tal curvas de attenuation in plumbo e in cemento esseva obtenite pro cesium 137.

Esseva constate que le radiation disperse se reduce plus o minus linearmente durante que le angulo de dispersion cresce usque a 90 grados sed que post iste puncto illo se reduce pauchissimo.

Le comparation del attenuation de disperse radios gamma de cesium-137 de un energie computate ab le relation de Compton con illo obtenite pro disperse radios gamma de cobalt-60 del mesme energia revelava un accordo sufficiente pro le computation de protection in general.

NATIONAL COMMITTEE ON RADIATION PROTECTION AND MEASUREMENTS

NEW RADIUM SOLUTION STANDARDS

The National Bureau of Standards has added a new series of 10^{-4}-and 10^{-11}-g radium standards to the list of radioactive samples it prepares and distributes. These radium solutions were prepared recently by W. B. Mann, L. L. Stockmann, and A. Schwebel of the Bureau's Radioactivity Section.[1] This new series was made up to restock the nearly depleted and less accurate 1940 supply of radium standards in this range. To provide standards with activities between the 10^{-9}-g and 10^{-11}-g values, new "blank solutions," containing 0.02×10^{-12} g of radium, have also been made available for dilution purposes.

These radium solution standards were issued as part of the Bureau's program to supply standards in all areas of the physical sciences. Radioactivity standard samples, such as these, are especially important, being widely used in the fields of physics, chemistry, biology, and medicine to control processes and maintain accurate equipment and apparatus.

NEW PUBLICATION

Announcement is made of a new publication, *Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and Water for Occupational Exposure*, National Bureau of Standards Handbook 69 (superseding Handbook 52), issued on June 5, 1959. The new Handbook contains 95 pages and the price is 35 cents.[2]

This Handbook includes the latest recommendations of the National Committee on Radiation Protection and Measurements (NCRP) concerning the maximum permissible internal exposure of the human body to radioisotopes. These recommendations represent a revision of those published by the NCRP in 1953.

The 1953 recommendations were for occupational exposure, twenty-four hours per day, continuously for seventy years. Prepared by the Subcommittee on Permissible Internal Dose, the study took five years to complete and included nearly 75 radioisotopes.

The work has continued at an accelerated pace since 1953 with the added co-operation of the International Commission on Radiological Protection (ICRP). The present Handbook includes maximum permissible concentrations (MPC) and body burdens for some 240 radioisotopes and includes many refinements based on knowledge not available in the earlier year. The study has included the evaluation of nearly 2,000 separate researches reported in the literature, having bearing on the permissible dose problem.

The new values reflect, where applicable, the lowering of the basic maximum permissible dose (MPD) recommended by the NCRP in 1957 and 1958. As a result of all these considerations, some values have been increased, some decreased, and others remain essentially the same. In addition, the calculations have been changed from seventy years continuous occupational exposure to fifty continuous occupational exposure, a more realistic figure for radiation workers. All maximum permissible concentrations (MCP) are given for both 40- and 168-hour weeks.

The recommendations in this Handbook are to be considered only as recommendations of a group of experts in the radiological protection field. They carry no legal force requiring or demanding adoption.

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[1] Mann, W. B., Stockmann, L. L., Youden, W. J., Schwebel, A., Mullen, P. A., and Garfinkel, S. B.: Preparation of New Solution Standards of Radium. J. Research NBS **62**: 21, 1959. RP2924.

[2] Order from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. Foreign remittances must be in U. S. exchange and should include an additional one-fourth of the publication price to cover mailing costs.

EDITORIAL

Radiation Biology

The Symposium on Radiation Biology presented at the Forty-fourth Annual Meeting of the Radiological Society of North America provided a broad and eclectic review of this rapidly evolving field for members of the radiological profession. The Symposium comprised two papers on radiation carcinogenesis and on late somatic effects of radiation, respectively, and four papers dealing with cell renewal and radiation injury, with possible additive or synergistic effects of combining chemotherapeutic agents with radiotherapy, and with the possible amelioration of radiation damage by one of the newer hormonal agents. The latter four papers appear in this issue of RADIOLOGY. A second symposium dealt with the hazards of radiation exposure in diagnostic roentgenology and the methods by which such exposure might be reduced.[1]

Such symposia can serve a most useful purpose by helping the radiologist keep abreast of developments in this sometimes bewildering field. Three different lines of investigation are generally subsumed under the heading "Radiation Biology": (1) the possible hazards of diagnostic and other medical uses of radiation; (2) the mechanism by which radiation kills normal and malignant cells, and the modification of these effects; (3) the assessment, treatment, and prevention of somatic and genetic injury to whole populations due to radiation from nuclear weapons testing, civilian medical applications, and natural background sources. The first of these areas, to which the public at large has now been alerted by a number of reports (1, 2, 3), is of particular interest to the diagnostic radiologist; the second is obviously the concern of the therapeutic radiologist; and it is clearly the responsibility of all radiologists to be conversant with the third, inasmuch as the public and our medical colleagues look to members of our specialty for authoritative opinions on all questions in this area.

The evaluation of possible hazards of small radiation doses in large populations is a tricky and difficult subject for investigation (4, 5, 6), and the radiologist must be alert to the statistical, dosimetric, and epidemiologic pitfalls with which it is beset. Our training has given us little preparation for dealing with these topics, and yet we are better prepared than the rest of our medical colleagues, who therefore look to us for help. Symposia which provide us with the timely, carefully considered views of experts in this branch of radiation biology may help us to fulfill this obligation.

The enhancement of awareness, *per se*, among members of our profession regarding sources of unnecessary and possibly excessive radiation exposure in the course of diagnostic x-ray examinations has done much to provide solutions to the problem. The discontinuance of examinations for which no clear medical indication exists, the avoidance of elective procedures in children and pregnant women, the use of gonadal shields and of filters and improved collimating devices should collectively reduce the level of exposure during the reproductive age period to levels which might be expected to placate even our geneticist colleagues (7).

Finally, there exists the real and exciting possibility that improvement in the end-results of radiation therapy for cancer may come through a better under-

[1] See Radiology **72**: 481–531, April 1959.

standing of the fundamental mechanisms by which radiation destroys normal and malignant cells. It is a tribute to the radiological profession that so much has been achieved in radiotherapy during the past sixty years, when such great reliance had to be placed on the slow process of trial and error. Today, however, a variety of new experimental technics have opened the door to further exploration of the fundamental mechanisms by which radiation acts at the cellular level (8). New methods of cell culture (9) have made possible an accurate appraisal of the injury to reproductive potential sustained by individual cells in an irradiated population. Advances in the biochemistry of the nucleic acids and proteins have provided a better understanding of their functions and interrelationships in the cell (10). Improved cytologic technics have made it possible to detect fine chromosomal lesions, as well as more bizarre abnormalities of chromosome number and morphology which are now known to occur in many cancer cells and may well have important implications for the prognosis of individual tumors (11). With the aid of microbeams of ionizing and ultraviolet radiation, the differential sensitivity of various parts of the cell, and even of parts of the chromosome, may now be studied (12). Newer concepts of cell population dynamics have clarified the arithmetical relationships between stem cells and their more differentiated progeny (13), and provided the basis for a better understanding of the repair of normal tissues after therapeutic radiation. The well established role of oxygen as a modifier of radiosensitivity has great potential significance in radiotherapy (14, 15, 16). A conference on tissue oxygen and radiotherapy held at Burlington, Vermont, in August 1958, under the auspices of the Radiation Study Section, National Institutes of Health, explored many facets of this complex subject. These and other new avenues of research encourage the hope that the day may not be far off when it will become possible to enhance selectively the sensitivity of tumor cells or to favor the recovery of normal cells through chemical or immunologic means, and thus to achieve substantial improvement in the end-results of radiotherapy of cancer. We may therefore look forward to a long series of symposia such as these in the anticipation of learning the fruits of investigations employing these new and exciting technics.

HENRY S. KAPLAN, M.D.

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IN MEMORIAM

MERRILL CLARY SOSMAN, M.D.
1890–1959

With the passing of Merrill Sosman on March 28, 1959, Radiology lost a pioneer, a dedicated friend, and one of its most potent and stimulating influences.

Born in Chillicothe, Ohio, on June 23, 1890, the son of Francis and Mary Browning Sosman, Merrill Sosman received his A.B. degree in 1913 from the University of Wisconsin and his M.D. from Johns

Hopkins in 1917. Having committed himself to the Military while still in medical school, his first clinical experience was as resident physician at the U. S. Soldiers' Home Hospital in Washington, D. C. He then decided to join the regular Army, in which one of his early assignments, after indoctrination courses at the Army Medical School, was to the encampment at Camp Humphreys, Virginia. This was during the height of the influenza epidemic and he himself was stricken with the disease. By decision of the Surgeon General, his field of interest was directed thereafter toward roentgenology, and orders for overseas duty with the Army of Occupation were rescinded in favor of successive assignments to the Army Medical School and as roentgenologist at the Walter Reed Hospital. In 1921, he was assigned for nine months of additional training to the Massachusetts General Hospital under the great Dr. George W. Holmes. . . .the man whom he forever after regarded as his "chief."

It was during this period that Harvey Cushing, who felt in 1911 that the proposed Peter Bent Brigham Hospital would need x-ray rooms but no special skiagraphic analyst, cast a reoriented eye toward the Massachusetts General and initiated a sequence of events which culminated in the appointment of civilian Sosman as roentgenologist to the Brigham Hospital in 1922. To this institution and to the Harvard Medical School, he devoted virtually his entire professional career.

A gregarious scholar and a gregarious man, why Merrill Sosman left an indelible imprint on the lives of those with whom he came in contact, is hard to say. To the student in the reaches of the amphitheatre, he will perhaps be remembered as the teacher with a crisp message, a better than average aim with chalk, and an improbable but never-to-be-forgotten illustrative story. The casual visitor to his department may remember only his mounted "stethoscope," with tongue-in-cheek epitaph. The removed listener at national meetings may recall a man of uncommon intellectual discipline, to whom the shadows in black and white were but one avenue to their correct interpretation. Whatever the after-image, those who knew Merrill Sosman as a doctor will never forget that he was a radiologist.

During an era in which the field of roentgenology was on trial as an entity worthy of recognition apart from departments of medicine and surgery, Dr. Sosman relentlessly exploited the x-ray method as an aid to more precise and accurate clinical diagnosis. His bibliography does not contain lengthy reviews of vernier observations on the x-ray findings in any given disease, although he made them. Rather, it contains brief reports of new observations—often no more than experiences with a handful of cases, because his observations were that certain and that important. His classic descriptions of intracardiac calcification brought him no less prestige than did his writings on the x-ray treatment of pituitary tumors; both loaned stature and dignity to his chosen field.

Possessed of great work capacity, Dr. Sosman's approach was forever academic, particularly in the sense that every one of today's observations became the workable basis for tomorrow's experience. He channeled his interests along the lines of interest of his clinical colleagues, always with mutual benefit. A master showman, with a commanding voice, instant repartee and just the right number of props, his every productive hour taught somebody something about medicine in general and radiology in particular. Most of his teaching to his residents was indirect; for he had rigid pedagogic standards and calculated methods. But his effectiveness lay in that unusual gift of inspiring his trainees not to want to let him down.

The lighter side of Merrill Sosman saw him as a patron of good music, a radiographer of Christmas presents and wildlife (ranging from trilobites to game birds), and an ardent fishing and hunting enthusiast. Just as he brought a radiological message *to* all parts of the world, so did he bring back fish *from* all parts of the world.

During the later years of his life, Dr. Sosman's physical activities were threatened by the pneumonectomy which was to cure him of bronchogenic carcinoma. With characteristic durability and equanimity, he bounded back to undertake, after his official retirement from the Peter Bent Brigham and Harvard in 1956, a globe-circling medical lecture tour. Upon his return, he resumed a pivotal position as Professor Emeritus and Consultant in Radiology to the Massachusetts General Hospital—the latter a "reappointment" which bracketed a service to Harvard University that was largely responsible for the establishment of an autonomous Department of Radiology.

Dr. Sosman's tangible contributions to medicine and his honors are legion. The author or co-author of some eighty-six papers in scientific journals, he had served as President of the American Roentgen Ray Society, the Harvey Cushing Society, and the New England Roentgen Ray Society; as Chairman of the Section of Radiology of the American Medical Association; and as a member of the National Research Council. In successive years, 1947 and 1948, he was the Caldwell Lecturer of the American Roentgen Ray Society and the Carman Lecturer of the Radiological Society of North America. In 1957, he was awarded the Gold Medal of the latter organization.

On June 27, 1918, Dr. Sosman married Arline Adams who, along with a radiologist son, Dr. J. Leland Sosman, a daughter, Mrs. Barbara Munson, and six grandchildren, survive him.

The onset of his terminal illness, a cerebral hemorrhage, came on Feb. 12, 1959, just as he completed a lecture on his world travels. He was mercifully unaware of the ensuing six weeks before a peaceful death ended the full life and lucent career of Merrill Clary Sosman, M.D.

JAMES B. DEALY, JR., M.D.

EDWARD SMITH BLAINE
1882–1958

Dr. Edward Smith Blaine, who had practiced radiology in Los Angeles for twenty-seven years, died at his home in San Marino, California, on Oct. 8, 1958.

Dr. Blaine was born in Chicago, Illinois, Dec. 16, 1882, was graduated in medicine from Marquette University in 1911 and, after a tour of European study, began his radiologic practice in Milwaukee as roentgenologist to Trinity and St. Joseph Hospitals. He moved to Chicago in 1914, and was, in succession, Director of Roentgenology for Cook County Hospital, West Suburban Hospital, and the Garfield Park Hospital. For five years he was head of the X-ray Department of Wesley Memorial Hospital. In 1931 he moved to Los Angeles, practicing radiology there until his death. He was Associate Professor of Roentgenology at Northwestern University from 1915 to 1930 and taught in the College of Medical Evangelists at Los Angeles from 1935 to 1944. He served in the Medical Reserve Corps as captain, major, and lieutenant-colonel. In the early phase of the first World War he was commanding officer of the Chicago School of Military Roentgenology and later was on the teaching staff at Camp Greenleaf.

Dr. Blaine was a member of the American Roentgen Ray Society and of the Radiological Society of North America. In the earlier years of his practice as roentgenologist, he made a number of important contributions to the radiologic literature, including a method of localization of foreign bodies and articles on fracture of the skull and on the roentgen aspects of osseous pathology. He was especially interested in orthophonic spelling and invented and copyrighted a sound spelling alphabet.

JAMES T. CASE, M.D.

JAMES NEWTON COLLINS, M.D.
1895–1959

Dr. James Newton Collins of Indianapolis died Jan. 3, 1959, of a coronary artery occlusion.

Jim Collins was born in Fayette, Alabama, in 1895. He received his A.B. degree from the University of Alabama and his M.D. from Emory University Medical School. After his internship, he spent two years in the study of radiology at the University of Michigan, while Dr. Preston M. Hickey was Chief of the Department of Radiology there. He then went to Indianapolis, where he joined the group of Drs. Cole, Beeler, and Smith, gaining a reputation as a therapist. He was on the staff of St. Vincent's and Methodist Hospitals and was Associate Professor, Department of Radiology, Indiana University School of Medicine.

Dr. Collins was active in all medical circles. He was a member of his county and state societies and of the American Medical Association. He was an active member of the Radiological Society of North America and served several years on the Scientific Exhibit Committee. He was a member, also, of the American Roentgen Ray Society and for many years was Secretary-Treasurer of the Indiana Roentgen Society. He was affiliated with the Second Presbyterian Church.

Surviving Dr. Collins are his wife, Josephine Washburn Collins; a daughter, Jane Collins Wilkerson; a son, Steven W., and one grandson.

Doctor Collins was exceptionally well grounded in the physical aspects of his specialty. He was the author of several medical papers, most of which dealt with the subject of roentgen therapy, a field in which he was well known and respected throughout Indiana. Radiology, particularly the private practice of radiology, has lost a valuable servant.

RAYMOND C. BEELER, M.D.

GOTTWALD SCHWARZ, M.D.
1880–1959

Dr. Gottwald Schwarz, eminent physician and pioneer in radiology, passed away in New York on Feb. 26, 1959, at the age of seventy-eight.

Dr. Schwarz was born in Brünn in old Austria-Hungary (now Czechoslovakia) on Aug. 2, 1880, moved to Vienna in his early childhood, and in 1904 was graduated from the Medical School of the University of Vienna. His interest in radiology dated back to his student days. During this period, he published an article on the effect of radium on the chicken egg, arriving at the conclusion that the biological effects of radiation were to be traced to a disintegration of lecithin. A short time after his graduation he presented a paper on the calomel-reaction of x-rays and its application to the measuring of x-ray doses. He wrote, also, on methods of decreasing and increasing the sensitivity of the skin to irradiation and was one of the first to explore the influence of x-rays on the blood and blood-forming organs.

Dr. Schwarz became one of the closest associates of the young Guido Holzknecht, and they, together

with Kienböck, can justly be called the fathers of the European school of roentgenology. With Holzknecht, Dr. Schwarz engaged in exploration of the diagnostic possibilities of x-rays in the study of the chest. Several papers bear witness to these investigations.

An appointment as Chief of the X-ray Department at the University Hospital of Vienna for Internal Diseases followed. During this period Dr. Schwarz published a number of papers on his experiences in the detection of gastric tumors and ulcers, and of stenoses of the small and large intestines, by means of x-rays. He reported, also, his observation of pulsation of the hilar shadows during fluoroscopy, thereby settling the controversial question of the times, as to whether the hilar markings represented vessels or ramifying bronchi. It was during this period that Dr. Schwarz's important scientific investigations on the barium enema were presented. Haenisch had made use of it for the purpose of diagnosis in 1911, but it was Schwarz who raised it to a level of greater precision and refinement, employing it particularly for the demonstration of high-seated lesions of the colon. He presented his clinical experiences on the pathology of the colon in a splendid monograph, which also set forth his profound physiological studies on the movement of the contents of the colon. He is represented in Schittenhelm's textbook, in the section dealing with the x-ray examination of the digestive tract.

In 1914 Dr. Schwarz was appointed to the Faculty of the Medical School of the University of Vienna, where he later became Professor. About 1920 he was made Director of the Department of Radiology at the Elizabeth Hospital in the same city.

His keen mind produced about 170 publications, among them several books. Approximately one-half of his papers were concerned with the scientific investigation of problems of diagnostics and the other half with questions on therapeutics, dealing primarily with radiobiological matters. His interest was particularly engaged in the changes within the tumor cell, especially its nucleus, under the influence of irradiation. Several years before Coutard, he made up his mind to treat certain tumors with fractionated doses to expose the neoplastic cells to irradiation "in the favorable period."

In 1910 Dr Schwarz was elected honorary member of the American Roentgen Ray Society. In 1937 he attended the International Congress of Radiology of Chicago as a delegate of the Austrian X-ray Society, of which he was co-founder and later honorary member. Owing to the political events in Austria he was forced to leave his native country in 1938 and came *via* London to New York, where he settled and maintained a private office, aided by his wife. In 1954 he was elected honorary member of the Medical Circle of New York and an active member of the New York Academy of Sciences. His wife, always his faithful companion, was his indispensable support and in his last illness an untiring devoted nurse.

Dr. Schwarz's outstanding work in radiology was not his only activity. He was strongly attracted by literature and music and wrote a number of novels and dramas, mostly with a background of ancient Roman history.

In Dr. Schwarz we have lost a cultured, fair-minded, brilliant personality, whose life work will be of enduring value. To Mrs. Charlotte Schwarz and her son, Dr. Gerhart S. Schwarz, radiologist, we extend our deepest sympathy.

MAX SGALITZER, M.D.

ANNOUNCEMENTS AND BOOK REVIEWS

AMERICAN BOARD OF RADIOLOGY

The Board of Trustees of the American Board of Radiology has decided to postpone the obligatory examination in Nuclear Medicine until after June 30, 1962, for those candidates being examined in Radiology or Therapeutic Radiology. Up until that time, therefore, the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology.

H. Dabney Kerr, M.D., Secretary.

GEORGIA RADIOLOGICAL SOCIETY

At the Spring meeting of the Georgia Radiological Society the following officers were elected for the coming year: Bert H. Malone, M.D., Brunswick, President; J. Frank Walker, M.D., Atlanta, Vice-President; George W. Brown, M.D., 317 S. 8th St., Griffin, Secretary-Treasurer.

RADIOLOGICAL SOCIETY OF HAWAII

The Radiological Society of Hawaii has recently elected the following officers, all from Honolulu: President, Col. Henry Harrell, M.C.; Vice-President, Capt. Paul Siebert, M.C.; Secretary-Treasurer, Louis L. Buzaid, M.D., Queen's Hospital, Box 861.

KINGS COUNTY RADIOLOGICAL SOCIETY

Newly elected officers of the Kings County Radiological Society (New York) are: President, Ernest Melton, M.D.; Vice-President, Aaron Tolk, M.D.; Secretary-Treasurer, C. Philip Naidorf, M.D., 411 Parkside Ave., Brooklyn 26, N. Y.

MARYLAND RADIOLOGICAL SOCIETY

A merger has recently been effected of the Radiological Section of the Baltimore City Medical Society into the larger Maryland Radiological Society. At the recent annual meeting of the parent group, the following officers were elected: President, Dr. Thomas R. Reid, Frederick; Vice-President, Dr. Nathan B. Hyman, Baltimore; Secretary, Dr. Albert B. Shackman, 705 Medical Arts Bldg., Baltimore 1; Treasurer, Dr. Howard Franz, Baltimore; President of the Executive Committee, Dr. Charles Davidson, Baltimore; Members of the Executive Committee, Dr. Webster Brown, Baltimore, and Dr. John Green, Easton.

MEMPHIS ROENTGEN SOCIETY

The Memphis (Tennessee) Roentgen Society at a recent meeting elected the following to office: President, Edward H. Mabry, M.D.; Vice-President, John M. Wilson, M.D.; Secretary-Treasurer, Hollis H. Halford, M.D., Kennedy VA Hospital, Memphis 15.

NEW YORK ROENTGEN SOCIETY

The New York Roentgen Society has chosen the following officers for the coming year: Harold G. Jacobson, M.D., President; Frank J. Borrelli, M.D., Vice-President; William B. Seaman, M.D., 622 W. 168th St., New York 32, N. Y., Secretary; Albert Dunn, M.D., Treasurer; Member of Executive Committee, John A. Evans, M.D.

PITTSBURGH ROENTGEN SOCIETY

At a recent meeting of the Pittsburgh (Pennsylvania) Roentgen Society the following officers were elected for the ensuing year: Lewis E. Etter, M.D., President; Theron B. Childs, M.D., Vice-President; Charles N. Chasler, M.D., Elizabeth Steel Magee Hospital, Pittsburgh 13, Secretary; Julius W. Ambrose, M.D., Treasurer.

SOCIEDAD VENEZOLANA DE RADIOLOGÍA

The Sociedad Venezolana de Radiología has recently elected a new administrative council as follows: President, Dr. José J. Fernández Carroz; Vice-President, Dr. César Herrera Pinto; Secretary-General, Dr. Rubén Merenfeld, Apartado postal 9362, Candelaria, Caracas; Recording Secretary, Dr. Luis A. Muro; Treasurer, Dr. Luis E. Gámez; Vocales, Dr. Diego Núñez Campos and Dr. P. M. Itriago Sifontes.

COURSE IN GASTROINTESTINAL RADIOLOGY, UNIVERSITY OF MINNESOTA

The University of Minnesota announces a continuation course in Gastrointestinal Radiology for radiologists to be held on the University campus Nov. 2–6, 1959. Guest participants will include Drs. John R. Amberg, Marquette University School of Medicine, Milwaukee; Edward B. Benedict, Harvard Medical School, Boston; Frank L. Campeti, University of Rochester School of Medicine and Dentistry, Rochester, N. Y.; Roberto L. Estrada, Montreal General Hospital, Montreal, Que.; Cesare Gianturco, Carle Hospital Clinic, Urbana, Ill.; Ross Golden, University of California School of Medicine at Los Angeles; Elliott C. Lasser, University of Pittsburgh School of Medicine, Pittsburgh; Richard H. Marshak, Mount Sinai Hospital, New York City; Harry Z. Mellins, State University of New York College of Medicine, Brooklyn; Everett L. Pirkey, University of Louisville School of Medicine, Louisville, Ky.; M. H. Popple,

New York University College of Medicine, New York City; Leo G. Rigler, University of California School of Medicine at Los Angeles; J. Maurice Robinson, University of California School of Medicine and Stanford University School of Medicine, San Francisco; Richard Schatzki, Harvard Medical School, Boston; Robert Shapiro, Hospital of St. Raphael, New Haven, Conn.; Frederic E. Templeton, University of Washington School of Medicine, Seattle; Sölve Welin, Allmänna Sjukhuset, Malmö, Sweden; Robert E. Wise, Lahey Clinic, Boston.

The Course will be presented under the direction of Dr. Harold O. Peterson, Professor and Head of the Department of Radiology; Dr. Joseph Jorgens, Associate Professor, Department of Radiology, and Chief of the Radiology Service, VA Hospital; Dr. Norman Blank, Instructor, Department of Radiology. The remainder of the Faculty will include members of the Faculty of the University of Minnesota Medical School and the Mayo Foundation.

Lodging and meal accommodations will be available at the Center for Continuation Study.

UNIVERSITY OF ROCHESTER SECOND CINEFLUOROGRAPHY SYMPOSIUM

The Second Annual Symposium on Cinefluorography will be held Friday and Saturday, Nov. 13-14, 1959, at the University of Rochester Medical Center, Rochester, New York. This Second Symposium will emphasize the clinical and investigative value of cineangiocardiography. Dr. Frank L. Campeti will give the Second Annual Cinefluorographic Lecture on Clinical and Investigative Studies.

Time will be provided for the presentation of information on image intensifier equipment, photographic technic and apparatus, and papers dealing with other clinical uses of cinefluorography.

Descriptions of cinefluorograms to be shown, abstracts of papers, and inquiries for further information should be addressed to Dr. George H. Ramsey, Department of Radiology, Strong Memorial Hospital, Rochester 20, N. Y.

QUEENS HOSPITAL CENTER

A course in Operative Radium Therapy is being offered by the Queens Hospital Center, Department of Hospitals, New York, commencing Saturday, Oct. 24, 1959, and continuing for eight successive Saturdays, from 9 A.M. to noon. Tuition for the course in $100.00.

Requests for applications should be sent to Dr. Philip Kahan, Supervising Medical Superintendent, Queens Hospital Center, 82-68 164th Street, Jamaica 32, N. Y.

Letter to Editor

To the Editor of Radiology

DEAR DOCTOR DOUB:

I've been studying Dr. Ira Kaplan's essay in the April issue of RADIOLOGY, together with the Discussion.[1] Dr. Friedell called attention to the fact that mutations are expected to be mostly recessive and that these are unlikely to show in the first generation except in the unpaired chromosomes, *i.e.*, in males. He called attention to the fact that Kaplan's 12 postnatal deaths were all in males, and that this is an unlikely coincidence. It is indeed—<1:1000. However, we can drop the indictment of possible radiation-induced mutation as the cause of death in 5 of the fatalities, namely, the 2 automobile accidents, the case in which there was a known history of familial disease, 1 death from tetanus, and 1 from drowning. This leaves 7, including 3 in children reported congenitally defective. The chance of 7 males without female is 1 per cent. We ought to be conditioned to accept infrequent coincidences by the success of the other 4 (I count 5) in beating the odds, too.

The observed defects, namely, extra finger, fingers wanting, and synostosis cranii, are usually taken to be nonhereditary, but rather accidents of development due to some intrauterine or vitamin lack, etc.

It was not brought out that 4 per cent of babies on the average show some congenital defect, half of which are presumably genetic. Among Kaplan's 566 children were 7 congenital defects (3 hydrocephalus, 1 Hirschsprung's disease, 1 Tay-Sachs, and 2 unspecified). This is 1.2 per cent. There were 12 deaths of living children, the eldest being six years old. This is 2.1 per cent. The ordinary mortality in the first year of life is about 3.5 per cent, in the first six years about 4.5 per cent.

Kaplan takes these observations as reassuring. For me, they serve to confirm my opinion that we who are concerned about radiation hygiene are talking about degrees or likelihood of injury that are unobservable. We shall continue to make decisions on the basis of extrapolations from observations that can be made on animals.

An absorbed dose of 65 r in the ovaries is calculated to double the natural mutation rate. For first generation observation, best look for dominant mutations. Let's look for achondroplasia in 80 per million per generation instead of the reported 40. Kaplan collected observations on 1/2000th of a million babies. I'm not making fun. I do value highly Dr. Kaplan's conscientious collection of data. But we have a long way to go before we reach validation in man of our extrapolations from mice.

Sincerely,
R. R. NEWELL, M.D.

[1] Genetic Effects in Children and Grandchildren of Women Treated for Infertility and Sterility by Roentgen Therapy.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

LOW INTENSITY RADIUM INTENSITY. By CHARLES L. MARTIN, E.E., M.D., F.A.C.R., Director of the Martin X-ray and Radium Clinic; Radiologist to Gaston Hospital; Consulting Radiologist to Parkland, Baylor and Veterans Hospitals; Clinical Professor of Radiology, Southwestern Medical School of the University of Texas, Dallas, Texas, and JAMES A. MARTIN, M.D., F.A.C.R., Associate Director of the Martin X-ray and Radium Clinic; Radiologist to Gaston Hospital; Consultant Radiologist to Parkland Hospital; Associate Professor of Radiology, Southwestern Medical School of the University of Texas, Dallas, Texas. A volume of 298 pages, with 20 color plates and 118 black and white illustrations. Published by Little, Brown & Co., Boston, Mass., 1959. Price $12.50.

A SHORT TEXTBOOK OF RADIOTHERAPY FOR TECHNICIANS AND STUDENTS. By J. WALTER, M.A., B.M. (Oxfd.), M.R.C.P. (Lond.), F.F.R., D. M.R.E. (Camb.), Clinical Teacher in Radiotherapy, University of Sheffield, Deputy Medical Director, Sheffield National Centre for Radiotherapy, Consultant Radiotherapist, United Sheffield Hospitals and Sheffield Regional Hospital Board, and H. MILLER, M.A., Ph.D. (Camb.), F.Inst. P., Chief Physicist, Sheffield National Centre for Radiotherapy, Hon. Lecturer in Radiological Physics, University of Sheffield. A volume of 528 pages, with 303 figures. Published by Little, Brown & Co., Boston, Mass., 2d ed., 1959. Price $10.00.

INTRACRANIAL CALCIFICATION. By FERMO MASCHERPA, Chief of the X-ray Department, Milan Neurological Institute, Milan, Italy, and VINCENZO VALENTINO, Radiologist of the Institute of Semeiological Medicine, Naples University; Neuroradiologist of the Hospital "A Cardarelli," Naples, Italy. A monograph of 150 pages, with 98 figures. Published by Charles C Thomas, Springfield, Ill., 1959. Price $9.50.

AN ATLAS OF NORMAL RADIOGRAPHIC ANATOMY. By ISADORE MESCHAN, M.A., M.D., Professor and Director, Department of Radiology, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C.; Consultant, Walter Reed Army Medical Center, Washington, D. C.; Formerly Professor and Head of the Department of Radiology, University of Arkansas School of Medicine. With the assistance of R. M. F. FARRER-MESCHAN, M.B., B.S. (Melbourne, Australia), M.D., Research Associate, Department of Radiology, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C. A volume of 760 pages, with 1,446 illustrations on 412 figures. Published by W. B. Saunders Co., Philadelphia, Penna., 2d ed., 1959. Price $16.00.

CEREBRAL ANGIOGRAPHY IN THE MANAGEMENT OF HEAD TRAUMA. By CHARLES A. CARTON, M.D., Formerly Assistant Professor of Neurosurgery, Baylor University College of Medicine, Chief of Neurosurgery, Veterans Administration Hospital, Houston, Texas; now Chief, Division of Neurosurgery, Montefiore Hospital, and Associate Clinical Professor of Surgery (Neurosurgery), Albert Einstein College of Medicine, New York, N. Y. A monograph of 158 pages, with 44 figures and a tabular Summary of Case History. Published by Charles C Thomas, Springfield, Ill., 1959. Price $7.00.

PRINCIPLES OF RADIATION DOSIMETRY. By G. N. WHYTE, National Research Council, Ottawa, Canada; Queen's University, Kingston, Ontario. A monograph of 124 pages, with numerous figures and tables. Published by John Wiley & Sons, Inc., New York 16, N. Y., 1959. Price $7.00.

MEDICAL RADIOGRAPHIC TECHNIC. Prepared by Technical Service, X-Ray Department, General Electric Company, under the original editorial supervision of the late GLENN W. FILES. Revision by WILLIAM L. BLOOM, JR., JOHN L. HOLLENBACH, R.T., JAMES A. MORGAN, R.T., and JOHN B. THOMAS, R.T. A volume of 386 pages, with numerous figures and tables. Published by Charles C Thomas, Springfield, Ill., 2d ed., 1959. Price $11.00.

CLINIQUES RADIOLOGIQUES. PREMIÈRE SÉRIE: L'AGRANDISSEMENT RADIOGRAPHIQUE DIRECT DANS L'EXAMEN DE LA BASE DU CRÂNE ET DES MICROFRACTURES DU ROCHER. By Professor J. ROUSSEL, Chaire d'Électroradiologie clinique de la Faculté de Médecine de Nancy. With the collaboration of P. SCHOUMACHER, M. PERNOT, and R. POIRÉ. Preface by Professor P. Lamarque. A volume of 102 pages, with 59 figures. Published by Masson & Cie, 120, Boulevard Saint-Germain, Paris VI^e, France, 1959. Price 3,200 fr.

ANGIOCARDIOPNEUMOGRAPHIE ÉLARGIE: MÉTHODE D'OPACIFICATION VASCULAIRE GÉNÉRALE PAR VOIE VEINEUSE. By P. VIALLET, Électroradiologiste des hôpitaux (Alger), L. SENDRA, Chef de Clinique à la Faculté de Médecine d'Alger, L. CHEVROT, Ancien Chef de Clinique à la Faculté de Médicine

d'Alger, P. AUBRY, Chef de Clinique à la Faculté de Médicine d'Alger, and P. COMBE, Professeur agrégé à la Faculté de Médecine d'Alger. A volume of 110 pages, with 46 figures. Published by Masson & Cie, 120, Boulevard Saint-Germain, Paris VI[e], France, 1959. Price 4,400 fr.

TUMEURS BÉNIGNES DES OS ET DYSTROPHIES PSEUDO-TUMORALES. By ANDRÉ TRIFAUD, Professeur agrégé à la Faculté de Médecine de Marseille, Chirurgien des hôpitaux, and HENRI BUREAU, Interne des Hôpitaux de Marseille. With the collaboration of HENRI PAYAN, Professeur agrégé d'anatomie pathologique à la Faculté de Médecine de Marseille. Preface by Professor Michel Salmon. A volume of 280 pages, with 136 figures. Published by Masson & Cie, 120, Boulevard Saint-Germain, Paris VI[e], France, 1959. Price 4,200 fr.

Book Reviews

BONE TUMORS. By LOUIS LICHTENSTEIN, M.D., Chief Pathologist, General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles; Fellow, New York Academy of Medicine; Professor Extraordinario, National University of Mexico; Consultant in Bone Tumors, Tumor Tissue Registry of California Medical Association Cancer Commission; Consultant in Pathology, Los Angeles County Hospital; Consultant, City of Hope Medical Center. A volume of 402 pages, with 220 figures. Published by C. V. Mosby Co., St. Louis, Mo., 2d ed., 1959. Price $12.00.

In the Preface to the first edition of this volume on Bone Tumors the author wrote: "This book is the outgrowth of a long series of studies on primary tumors of bone pursued in collaboration with Dr. Henry L. Jaffe during the period 1938–1948." In this second edition, six years later, "the accrued observations and advances of the past several years have been incorporated in the subject matter presented, so that virtually every chapter has been modified to some extent." A chapter on "Tumors of Periosteal Origin" has been added. The Appendix, "Some Non-Neoplastic Lesions of Bone Which May Be Mistaken for Tumors," has been amplified, and a second Appendix has been introduced, on "Tumors of Synovial Joints, Bursae and Tendon Sheaths."

The author has done an exceptional task of clarifying the classification of bone tumors. Such ambiguous diagnoses as chondro-osteosarcoma or osteochondrosarcoma are completely excluded. More accurate diagnosis is emphasized, so that each tumor can be recognized by its distinctive features, thus affording a basis for appropriate treatment.

The newer entities, as benign chondroblastoma, chondromyxoid fibroma, and benign osteoblastoma of bone, are well demonstrated and individually separated as distinct bone neoplasms. The author includes a discussion of the controversial "Ewing's sarcoma of bone" with his opinion as to the cellular characteristics and clinical course differentiating it from primary reticulum-cell sarcoma of bone.

Each chapter is well organized, with a short general discussion of the subject material, followed by the clinical features, such as sex and age incidence, complaints, and localization. The roentgenographic and pathological observations are supplemented by good reproductions of roentgenograms, photographs of gross specimens, and photomicrographs. The discussions of treatment and prognosis leave no question as to the author's idea as to how the tumor is to be handled. Each chapter includes a brief summary.

This work is recommended as a guide to better evaluation of bone tumors for orthopedists, radiologists, and pathologists. This does not limit the book, however; it will prove of value to others who only occasionally encounter bone tumors and desire an authoritative, accurate short discussion of the problems involved.

TREATMENT OF CANCER AND ALLIED DISEASES. VOLUME I: PRINCIPLES OF TREATMENT BY FIFTY-FIVE AUTHORS. VOLUME II: TUMORS OF THE NERVOUS SYSTEM BY THIRTY AUTHORS. VOLUME III: TUMORS OF THE HEAD AND NECK BY SEVENTY AUTHORS. Edited by GEORGE T. PACK, M.D., F.A.C.S., Attending Surgeon, Memorial Center for Cancer and Allied Diseases; Associate Professor of Clinical Surgery, Cornell University Medical College; Surgeon, Pack Medical Group, New York, and IRVING M. ARIEL, M.D., F.A.C.S., Associate Clinical Professor of Surgery and Associate Attending Surgeon, New York Medical College, Flower and Fifth Avenue Hospitals; Surgeon, Pack Medical Group, New York. Volume I, 646 pages, with 505 figures; Volume II, 316 pages, with 340 figures; Volume III, 782 pages, with 1,028 figures. Published by Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York, N. Y., 2d ed., 1958 (Vol. I), 1959 (Vols. II and III). Price $22.50; $15.00; $30.00.

This series is a revision of the encyclopedic work on the treatment of cancer by Pack and Livingston, published in 1940. It represents an attempt to include in one authoritative work the tremendous mass of detailed information concerning all phases of cancer therapy in current use. The care of the patient is emphasized throughout, and palliative procedures are given the same emphasis as measures aimed at cure.

The presentation is regional in nature. Under each region are considered the treatment procedures best suited for a given histologic type of cancer.

Volume I discusses principles of cancer treatment and various ancillary subjects such as biopsy, pre- and postoperative care, etc. Volume II is devoted to the nervous system, and Volume III to the head and neck. These three volumes have been published and are reviewed herewith. The remaining six volumes will be reviewed as they appear. They are: Volume IV on the treatment of tumors of the breast, chest, and esophagus, Volume V concerning tumors of the gastrointestinal tract, Volume VI dealing with the treatment of cancer of the female genitalia, Volume VII on cancer of the male genital tract and the urinary system, Volume VIII on tumors of the soft somatic tissues and bone, and Volume IX on treatment of tumors of the skin and of lymphomas and allied diseases.

Each volume contains contributions from recognized authorities on neoplastic disease in many parts of the world, and an effort has been made to present time-proved methods of therapy in each case. Controversial subjects have been discussed from both sides and, while it is inevitable that there be some conflicts of opinion, an effort has been made to set forth the facts from which the reader can draw his own conclusions. The emphasis throughout is on practical procedures. While surgery and radiation are stressed as therapeutic modalities, chemotherapy and hormone therapy and other therapeutic agents receive full consideration where pertinent.

Volume I. Principles of Treatment: This volume is intended as an introduction to the series, and a reference for general principles of use of the various modalities. It opens with a section on organization of cancer clinics and a home-care program. A section presenting the general features of cancer diagnosis is followed by one on surgery which is particularly concerned with estimation of risk, pre- and postoperative care, and special surgical technics of importance in cancer treatment. There are several sections on radiation therapy which give background information of particular interest to the nonradiologist. Hormone therapy, chemotherapy, and general care of the cancer patient are considered in the next section, and the volume closes with a discussion of the problems in reporting end-results of treatment.

Volume II. Tumors of the Nervous System: Volume II, the thinnest of the three volumes yet published, is concerned with the treatment of tumors involving the brain, spinal cord, and the peripheral nerves. In this region, the greatest emphasis is on surgical treatment, but there is adequate discussion of radiotherapeutic technics to preserve a reasonable balance.

The first few chapters are introductory, dealing with classification, aids to diagnosis, general principles of surgical and radiation treatment, pre- and postoperative care, and anesthesia. These are followed by a systematic presentation of treatment of various tumor types and locations. Chapters are included on gliomatous tumors, pituitary adenomas, meningiomas, vascular tumors, lymphomas, etc. There is also consideration of tumors of the spinal cord and of the peripheral nerves. The volume closes with discussions of prefrontal lobotomy and other surgical procedures for the relief of pain.

Volume III. Tumors of the Head and Neck: Tumors of the head and neck constitute a group in which both radiation and surgery have a curative role. There is perhaps more controversy regarding the relative merits of the two modalities in this region than in any other. The editors have chosen a middle course by their choice of subject and contributor and offer a fairly well balanced picture, though from the point of view of the radiation therapist, the balance favors surgery in some instances.

After a section on general principles, including routes of spread, anesthesia, and pre- and postoperative care, sections are devoted to tumors of the mouth, pharynx, nose, and sinuses, tumors of the eye, and tumors of the ear. There is an excellent discussion of tumors of the larynx, with full emphasis on the value of radiation. The section on tumors of the neck includes the treatment of lymph node metastases. The final section in this volume concerns tumors of the thyroid and parathyroid glands.

These volumes represent a good review of current attitudes toward therapy of cancer in the regions so far discussed. The books are very well finished with excellent illustrations, but are quite expensive. The cost of the whole series will be formidable, which may restrict its distribution chiefly to libraries. It is a good reference work on cancer therapy.

ATOMIC MEDICINE. Edited by CHARLES F. BEHRENS, M.D., F.A.C.R., Rear Admiral, MC, U. S. Navy (ret.); Roentgenologist, Yater Clinic-Washington, D. C.; Consultant and Lecturer in Radiology, U. S. Naval Medical Center, Bethesda, Md. Formerly: Director, Atomic Defense Division, Bureau of Medicine and Surgery, Navy Department; Commanding Officer, Navy Medical Research Institute, National Naval Medical Center, Bethesda, Md. A volume of 706 pages, with figures and tables. Published by Williams & Wilkins Co., Baltimore, Md., 3d ed., 1959. Price $15.00.

This is the third edition of a comprehensive work on atomic medicine written by a distinguished group of authors under the direction of Rear Admiral Behrens. In view of the many advances in this field some chapters have been rewritten and new ones have been included. A considerable amount of discussion on radiation hazards has been added. Some of this relates to bomb effects and some to fallout. The problem of acute whole-body radiation is thoroughly discussed.

A relatively small portion of the text is devoted to physics and nuclear weapons. Considerable emphasis is placed on biological and clinical studies of ionizing radiation and radiation injury, and attention is drawn to protective measures. The medical aspects of radioisotopes of various types are covered, with special emphasis on radiophosphorus and radioiodine. The design and operation of radioisotope laboratories also receive attention. Extensive references are given at the end of each chapter.

This book contains a wealth of information for all physicians who wish to keep abreast of the newer developments in nuclear medicine.

RADIOLOGY FOR MEDICAL STUDENTS. By FRED JENNER HODGES, M.D., Professor and Chairman, Department of Radiology, University of Michigan, ISADORE LAMPE, M.D., Professor, Department of Radiology, University of Michigan, and JOHN FLOYD HOLT, M.D., Professor, Department of Radiology, University of Michigan. A volume of 450 pages, with 107 plates. Published by the Year Book Publishers, Inc., Chicago, Ill., 3d ed., 1958. Price $8.50.

This book, the third edition of a text first published in 1947, is recommended to any reader interested in an introduction to the field of radiology. It is intended primarily for undergraduate students of medicine and their teachers. There is excellent coverage of all aspects of this specialized field, which combines general medicine and a knowledge of electronics and physics.

Attention has been given to the newer developments in both diagnosis and treatment that have marked the decade since the original publication date. To the section on Diagnosis has been added a chapter on cardiovascular roentgenography and to the section on Radiotherapy new material on cobalt 60 as a source of high-energy gamma radiation. This latter section opens with a chapter entitled "General View of Therapeutic Radiology," which is a concise summary of the subject without the confusion of too many technical details. The remaining chapters give the reader a sound introduction to current treatment concepts.

PATIENT CARE AND SPECIAL PROCEDURES IN X-RAY TECHNOLOGY. By CAROL HOCKING VENNES, R.N., B.S., Formerly Surgical Supervisor and Clinical Instructor, University of Minnesota Hospitals, Minneapolis, Minn., and JOHN C. WATSON, R.T., Director of Courses in X-Ray Technology, University of Minnesota Hospitals, Minneapolis, Minn. A volume of 204 pages, with 62 figures. Published by the C. V. Mosby Co., St. Louis, Mo., 1959. Price $5.75.

Since the beginning of a formal training course in x-ray technology and the outline of a well defined curriculum, there has been a dearth of collected material for use in the teaching of nursing procedures and patient care to student technologists. These subjects have an important place in a well balanced training program but reference material has had to be garnered from textbooks written for student nurses, trainees, and other sources.

Carol Hocking Vennes, a registered nurse, in collaboration with John C. Watson, a registered technician, have written a fine handbook that is particularly adaptable for use in teaching the art of patient care. The text covers practically every phase of doctor-technician-patient relationship both in routine and specialized procedures, such as neuroradiography, vascular radiography, and the many other examinations being used in present day radiographic departments.

This text book should be a boon to training school instructors as well as all technicians who wish to keep abreast of present day procedures in an ever changing technology.

THE PHYSIOPATHOLOGY OF CANCER BY 32 AUTHORS. Edited by FREDDY HOMBURGER, M.D. Foreword by Joseph C. Aub, M.D., Sc. D. A volume of 1,180 pages, with 189 figures and 100 tables. Published by Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York 16, N. Y., 2d ed., 1959. Price $33.00.

This is a book designed to bring together the available knowledge on cancer research in its various aspects. Only a small portion is devoted to clinical applications. The chapters are written by thirty-two authors who are well known and thoroughly competent in their fields. In this second edition, seven new chapters have been added to bring the material up to date.

The text is divided into four main sections: (1) Biology (eleven chapters), (2) Chemistry and Physics (nine chapters), (3) Clinical Investigation (five chapters) and (4) Practical Applications (three chapters). Extensive bibliographies are appended to the various chapters. A general index aids in locating subjects for easy reference.

This book should be of great value to the student and those doing research in the basic aspects of the cancer problem.

GENETICS, RADIOBIOLOGY AND RADIOLOGY PROCEEDINGS, MID-WESTERN CONFERENCE. [Edited by] WENDELL G. SCOTT, M.D., Chairman; Chairman, Committee on Radiology, National Research Council, and TITUS EVANS, Ph.D., Co-Chairman; Member, Committee on Radiology, National Research Council. A volume of 150 pages with 21 figures. Published by Charles C Thomas, Springfield, Ill., 1959. Price $5.50.

This is a report of one of three regional meetings sponsored by the National Academy of Sciences-National Research Council and its Committee on

the Biological Effects of Atomic Radiation. Participants included four professors of genetics, four of radiobiology, and twenty-one of radiology.

The site and mechanism of radiation action and damage are first discussed, followed by a consideration of problems related to assessment of the dangers of mutation. Experiments on time-dose and the shape of the dose response curve, made to determine whether a threshold exists for genetic damage, are described and their significance explained. The discrepancy between results obtained on mice and extrapolation to this species of experimental observations on *Drosophila* is pointed out and extrapolation from mouse to man is discussed. The different aspects of the problem in male and female are described. The report closes with a consideration of means of decreasing the radiation received by the patient during diagnostic x-ray procedures.

With the current interest of the public in the dangers of radiation, the radiologist is expected to answer questions of patients and physicians in other fields. This little book will be of help in this respect.

L'OESOPHAGE: ACTUALITÉS HÉPATO-GASTRO-ENTÉROLOGIQUES DE L'HÔTEL-DIEU, 1957. [Edited by] GUY ALBOT, Médecin de L'Hôtel-Dieu and FÉLIX POILLEUX, Chirurgien de L'Hôpital Corentin-Celton. By A. AUBIN ET AL. A volume of 274 pages, with 112 figures. Published by Masson & Cie, 120, Boulevard Saint-Germain, Paris, VI^e, France, 1958. Price 3,600 fr.

This monograph on the esophagus is the outcome of one of a series of conferences in which internists, surgeons, radiologists, and other specialists have pooled their knowledge about specific fields. It opens with a chapter on technic of esophageal examination, including pertinent historical facts. Various conditions of interest, such as esophagitis, ulceration, carcinoma, diverticulum, caustic injury, hiatus hernia, and eventration are then discussed by the different specialists.

This is a good general review of diseases of the esophagus. Most of the material may be found in various publications in English. One unusual condition is mentioned, however, which is probably not known to any great degree in English speaking countries, namely, involvement by trypanosomiasis of the cardia and lower end of the esophagus in such a manner as to simulate cardiospasm or achalasia.

DERMATOLOGIE UND VENEROLOGIE: EINSCHLIESSLICH BERUFSKRANKHEITEN, DERMATOLOGISCHER KOSMETIK UND ANDROLOGIE IN FÜNF BÄNDEN. Edited by Prof. Dr. Dr. h. c. H. A. GOTTRON, Direktor der Universitäts-Hautklinik Tübingen, and Prof. Dr. Dr. h. c. W. SCHÖNFELD, Direktor der Universitäts-Hautklinik Heidelberg. BAND II/TEIL 1: PHYSIKALISCHE BEHANDLUNG, DERMATOLOGISCHE KOSMETIK, KRANKHEITEN NOCH UNBEKANNTER HERKUNFT NACH IHRER MORPHOLOGIE. Bearbeitet von W. Blaich, Wuppertal-Elberfeld, et al. A volume of 758 pages, with 388 figures, some of which are colored. Published by Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, Germany, 1958. Price DM 173.—($41.20); by subscription DM 138.40 ($32.85).

In this volume, which is part of a larger treatise on dermatology and venereology, there are several sections of direct interest to practicing radiation therapists. The introductory chapter on "General Principles of Physical Therapy" (pp. 1–25), by E. H. Graul and L. Rausch, is an excellent summary of current views on biologic effects of ionizing radiations, though perhaps a bit too technical for the rank-and-file dermatologist.

"Special Roentgentherapy" (pp. 26–132), by Albin Proppe, offers a good discussion on skin cancer (pp. 34–73), followed by a two-page intermezzo which carries the statement (quoted from Langendorff; Seelentag) that 1 r of (presumably total-body) radiation shortens by three to six days the average lifespan of an individual. Nevertheless the immediately following section on the roentgen treatment of "benign" skin conditions (pp. 75–125), is ten pages longer than the section devoted to malignant disease. It includes old-time standards—hemangioma, keloid, ringworm epilation, Peyronie's disease—as well as others which, particularly in this country, are regarded as questionable indications for irradiation (eczema, warts, psoriasis, inflammations). The section concludes with a subchapter on "indirect" roentgen therapy (pp. 119–125), by which is meant an attempt to influence the disease (the only present use of this method is apparently in lichen planus) by irradiating the sympathetic ganglion chain.

Proppe does not outrightly advocate radiotherapy in all these nonmalignant conditions but, with certain reservations, he still regards most of them as valid indications for the use of roentgen rays. Less objectionable are his etymologic preferences: he abuses the term "nosologic," which is an innocent habit, but he also wants to promote the term "basaloma," intended to remove the basal-cell tumors from the category of skin carcinoma. Conversely, his remarks on the treatment of malignant skin lesions are very judicious. He makes a valiant attempt to reconcile German and English-speaking authors with regard to melanoma, which is excised in this country but irradiated (without prior biopsy) in Germany. Proppe himself foregoes biopsy, irradiates the site of melanoma beyond a cancerocidal level and then, after the reaction has subsided, excises the lesion with a wide margin of skin, including all the irradiated portions.

The brief chapter on "Soft Roentgen Rays" (pp. 133–148), by Carl Georg Schirren, is mostly

technical. The author alleges that total-body irradiation, at 2 meters TSD, 50 kvp, and 25 ma, at 20 r/min, affects the skin exclusively. He recommends it up to a total of 300 to 600 r in eczema and erythroderma, up to 800 to 1,400 r in malignant reticuloses.

The chapter on "Radium" (pp. 149–165), by J. Tappeiner and P. Wodniansky, of Vienna, contains on page 156 the statement that radon "is being used" in the following manner: (a) for inhalation, (b) for drinking cures, and (c) for bathing and in compresses! Radium application is recommended first of all for inveterate staphylococcal infections (from paronychia to furuncles), but also in Dupuytren's contracture, in Peyronie's disease, and in various types of verruca, and, though perfunctorily, in cavernous hemangioma and carcinoma. In the latter instance, the sad remark is made that Chaoul's contact therapy has all but replaced the use of radium. As a surprise feature, these authors elaborate on the hazards of radium (pp. 161–164).

The betatron (pp. 166–187)—the German term is electron slinger (*Elektronenschleuder*)—is discussed in an interesting, though largely technical chapter by H.-G. Bode (who in 1950 was the first to use an electron beam to treat carcinoma) and B. Markus. With a 15-Mev Siemens installation, the electron beam produced suffices to treat in a single session any cancer which does not reach more than 2 cm. below the surfaces; with fractionated doses, the effective depth is said to approach 5 cm. Indications for electron beam therapy are melanoma, lymph node metastases, and any other deep-rooted, thick, and/or "radio-resistant" skin cancer.

In the chapter on "Artificial Radioactive Isotopes" (pp. 188–210), K. E. Scheer and H. J. Endres list among the beta-emitters Low-Beer's blotting-paper method with P^{32} and various Sr^{90} applicators, among the gamma-emitters Co^{60} incorporated in a resin-base (plastobalt), which facilitates the production of molds. Au^{198} is still the favorite for interstitial irradiation, but Co^{60}, Ir^{192}, or Ta^{182} are mentioned as future possibilities. So-called selective therapy is a term used to designate internal administration of P^{32} or other radioisotope (I^{131}, As^{76}) in the hope that it will be concentrated particularly by the tissues to be treated.

The outdated statements on radium and radon therapy, and other undesirable items, may have been preserved as "traditional" features in this ultra-comprehensive type of treatise. Care should be taken to remove them from future editions.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

BROADBRIDGE, A. T., AND LESLIE, E. V. Cerebral Angiographic Contrast Media: A Comparison of Hypaque 45% and Urografin 60% and an Assessment of the Relative Clinical Toxicity of Urografin 60%, Hypaque 45%, Diaginol 25% and Diodone 35% in Carotid Arteriography 286

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Cerebral Angiographic Contrast Media: A Comparison of Hypaque 45% and Urografin 60% and an Assessment of the Relative Clinical Toxicity of Urografin 60%, Hypaque 45%, Diaginol 25% and Diodone 35% in Carotid Arteriography. A. T. Broadbridge and E. V. Leslie. Brit. J. Radiol. **31:** 556–560, October 1958. (A.T.B., Royal Surrey County Hospital, Guildford, Surrey, England)

Four series, each of 200 unselected carotid arteriograms performed with Urografin 60 per cent, Hypaque 45 per cent, Diaginol 25 per cent, and Diodone 35 per cent, were analyzed with respect to neurological complications which could in any way be related to arteriography with these media. Ten cubic centimeters of medium was used per injection (since reduced to 7 c.c.), with an average of three injections per side. Thus in a bilateral examination, a total of 60 c.c. may have been used. The patients were closely observed by nurses trained in neurosurgery. Virtually all changes occurring within twenty-four hours were counted. The complication rate may therefore seem high.

"Minimal" complications included transient paresis or confusion, transient worsening of pre-existing complaint, and worsening of the general condition of a severely ill patient. The incidence was 11.3 per cent for Hypaque and 12.3 per cent for Urografin, a statistically significant increase over the other media.

"Significant" complications included onset of hemiplegia or sensory loss, and persistent worsening of a pre-existing complaint. The range of incidence was 0.7 to 3.5 per cent with no statistically significant difference for any one medium. There were no deaths attributable to arteriography nor were there any serious allergic reactions.

Sixty patients were examined bilaterally, with Hypaque 45 per cent on one side and Urografin 60 per cent on the other. There was a slight subjective preference for Urografin, but this advantage was offset by the greater viscosity of that medium. Hypaque and Urografin gave equal and excellent vascular contrast, which was superior to that obtained with the other two media, and they were no more irritating to the patient. It was therefore concluded that, in spite of the higher incidence of minor sequelae, use of Hypaque 45 per cent and Urografin 60 per cent in cerebral arteriography is justified.

One table.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Vertebral Arteriography in Neurosurgical Diagnosis. G. Ruggiero, A. Thibaut, and J. Bories. Acta radiol. **50:** 365–380, October 1958. (In French) (Hôpital Sainte-Anne, Paris, France)

This paper consists in a summary of the authors' experience in 227 arteriographic studies in 215 patients, 95 females and 120 males, done with Lindgren's technic I (Acta radiol. **33:** 389, 1950. Abst. in Radiology **56:** 604, 1951). In 148 of the most recently performed examinations, the percentage of failures was only 2.7. This represents as high a rate of success as is obtained by the catheterization method. The skill and experience of the operator are more important than the choice of needle or contrast medium in the outcome of the examination.

The authors give a statistical analysis of the results of their examinations under three main headings: vascular abnormalities, nontumoral hydrocephalus, cerebral tumors. Technical factors such as needles, contrast material, anesthesia, spasm, and untoward reactions are all discussed.

Fifteen roentgenograms; 3 tables.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

The Radiological Investigation of Intracranial Abscess. G. Kenneth Tutton and Robert Ollerenshaw. Brit. J. Radiol. **31:** 571–574, October 1958. (Manchester Royal Infirmary, Manchester, England)

This paper is a description and partial reproduction of a demonstration by the authors which received an award at the 1957 Annual Congress of the British Institute of Radiology. The exhibit consisted of sixteen 14 × 17-in. panels which were transilluminated. The subject was the radiological investigation of 83 cases of intracranial abscess. One panel giving the *raison d'etre* of the whole may be summarized as follows:

Radiology is chiefly of value in hematogenous cases (one third of series). In most abscesses due to direct spread, clinical signs render arteriography and ventriculography superfluous, though plain films may yield valuable information, such as the presence of gas in an abscess cavity, an area of bone destruction, or shift of the pineal.

A brain abscess with no obvious focus of infection is not infrequently regarded as a possible tumor and is hence subjected to routine investigation for a space-occupying lesion. In view of the frequency (one quarter of this series) of thoracic suppuration as a primary cause, the chest should be examined radiologically in all cases.

Aspiration of pus and instillation of 2 ml. of Thorotrast, together with the appropriate antibiotic, is the basis of present-day treatment. Subsequent serial pyograms permit the assessment of progress, the detection of developing loculi, and the decision whether to excise the abscess. In certain cases, especially where the abscess is loculated or where it lies deeply in the cerebellum, radiographic control of the actual process of needling has been found of value.

Eight of the panels including 26 roentgenograms and 8 photographs, are reproduced.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Iodoventriculography in Lesions of the Posterior Fossa. G. Cornélis, Hou-Hio-Hi, and R. Gonsette. J. belge de radiol. **41:** 548–575, 1958. (In French) (Université de Louvain, Belgium)

The authors describe a method of visualizing the third ventricle, aqueduct, and fourth ventricle after injection of a positive contrast material such as Lipiodol or Ethiodan. The injection is made through burr holes into the lateral ventricles and the medium is allowed to accumulate in the frontal horns whence it passes through the foramina of Monro into the third

ventricle, aqueduct, and fourth ventricle. The procedure is found helpful in diagnosing tumors of the posterior fossa and in the study of nonneoplastic obstructive lesions.

Twenty-three roentgenograms; 1 table.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Radiography of Aqueous Humor Outflow. Bruce E. Cohan. Arch. Ophth. **60:** 110–115, July 1958. (Ophthalmology Branch, National Institute of Neurological Diseases and Blindness, Bethesda 14, Md.)

In 1956, the author described a technic for radiography of the aqueous outflow mechanism in the rabbit, using water-soluble radiopaque materials (Arch. Ophth. **55:** 792, 1956. Abst. in Radiology **68:** 762, 1957). Multiple slit-lamp examinations of each eye in that series and subsequent histologic study revealed only a mild and transient response of the anterior segment to the contrast medium. Radiography is by far less damaging to the delicate ocular tissues than methods employing histologic sections or neoprene casts. It permits the investigator to study a functioning and essentially intact aqueous outflow system, particularly within the depths of the sclera.

In the present experiment 0.2 c.c. of 50 per cent sodium diatrizoate (Hypaque) was used to replace the same volume of aqueous. The technic was identical with that described in the preliminary report, with the following exceptions: The rabbits were placed in a lateral position for the filming, depth of anesthesia was more carefully controlled, and restraints, which in no way exerted pressure on either neck or eye, were employed. All roentgenograms were taken within twenty minutes of replacement of aqueous by the contrast solution. A specially constructed experimental x-ray tube was used.

The following anatomic details of the aqueous outflow system were demonstrated: From the ciliioscleral sinus (a cleft which communicates with the anterior chamber) numerous collector channels lead to the deep scleral plexus. Two outflow pathways originate from this plexus: first, communicating vessels rise through the sclera to emerge as aqueous veins; and second, anastomotic vessels extend to a plexus of veins in the ciliary muscle. This plexus communicates with the vortex venous system and, in addition, perforating vessels from it emerge on the scleral surface as laminary veins. Aqueous and laminary veins are tributaries of the anterior ciliary venous system.

Four roentgenograms; 5 drawings.

Intraocular Foreign Body. Arnold I. Turtz and Alfred Mamelok. Arch. Ophth. **60:** 132–136, July 1958. (525 Park Ave., New York 21, N. Y.)

A case is reported in which roentgen examination failed to reveal the presence of a relatively large intraocular foreign body. A 7-year-old boy was admitted to the hospital one hour after being struck in the left eye by a pencil. Examination showed a 5 mm. horizontal penetrating laceration of the left cornea, with laceration and prolapse of portions of iris and lens. The fundus could not be visualized, owing to corneal and lens changes. Routine x-ray examination disclosed no evidence of a foreign body. There was a good initial response to surgical treatment (excision of the prolapsed and incarcerated tissues, irrigation of the anterior chamber, and closure of the corneal laceration) and the administration of antibiotics. After two weeks, however, an apparent "escape" from therapeutic control occurred, with recrudescence of endophthalmitis. Despite all treatment, softening of the globe and loss of light perception ensued. About three weeks after the injury, evisceration of the globe was performed and a plastic sphere was implanted into the scleral shell. During the procedure a piece of pencil lead 15 mm. long was unexpectedly discovered.

Pencil "lead" is of course in reality graphite, a soft native carbon with metallic sheen. The comparative radiotransparency of carbon (0.480) approximates that of bone (0.560) when compared with iron (0.101) or lead (0.055). Therefore the presence of intraocular carbon foreign bodies can be demonstrated only by the bone-free technic of Vogt (Schweiz. med. Wchnschr. **51:** 145, 1921) or Lindblom (Acta ophth. **26:** 439, 1948. Abst. in Radiology **53:** 760, 1949). Lengths of graphite, 15 mm. long, from hard, medium and soft lead pencils were inserted into enucleated cat eyes through a small posterior stab incision. Routine anteroposterior and lateral roentgenograms taken with the eyes placed in the orbit of a skull failed to reveal the presence of the foreign bodies, which, however, were readily demonstrated by a bone-free technic.

It is suggested that the bone-free technic be employed in any case of suspected intraocular foreign body when routine studies are negative.

Six roentgenograms; 2 photographs.

Radioanatomic Study of the Anterior Condylar Canal. J. Metzger, M. Dary, and A. Wackenheim. J. de radiol. **39:** 640–644, October 1958. (In French) (Clinique Neurochirurgicale de la Pitié, Paris, France)

In a patient with a possible lesion of the hypoglossal nerve, the roentgen study may be performed according to various technics. One method calls for a frontal tomographic section with the incidence described by Herdner for the posterior foramen lacerum, or a tomographic section of the petro-spheno-occipital region may be indicated. Other technics are described in minute detail but are probably more difficult to apply in daily practice. In one which might be useful, the central beam enters at a point 1 cm. in front of and 1 cm. below the level of the maxillary inferior condyle, which means that it travels through the sigmoid notch and zygomatic arch. The point of exit is 1 cm. below and 3.5 cm. lateral to the external occipital protuberance. This projection shows the condylar canal quite clearly.

Five roentgenograms; 4 diagrams; 1 table.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Sialography in Children. Bromley S. Freeman. Surg., Gynec. & Obst. **107:** 505–507, October 1958. (Baylor University College of Medicine, Houston, Texas)

Contrast radiography of the major salivary glands is of diagnostic value in children with swellings in these areas, aiding in the differentiation of infections and tumors, intrinsic growths and extrinsic compression, and occasionally in planning (or preventing) exploratory surgery.

In preparing the patient, premedication is extremely important. Surface anesthesia of the duct opening with 2 per cent tetracaine hydrochloride is followed by probing and gradual dilatation of the tiny sphincter.

Following this a metal guarded syringe with a special needle is slipped in place and 0.8 to 1 cm. of Pantopaque is slowly injected to the point where the child complains bitterly of pain. The needle is left in the duct until just before the roentgen exposures.

It was found that over-injection is extremely painful, causes pathologic changes in the glands, and obscures the finer details on the films. The end-point of "bitter pain" was used for the injection, but never was 1.5 c.c. exceeded.

Five brief case reports are presented.

Six roentgenograms; 2 photographs.

CARL KAPLAN, M.D.
University of Pennsylvania

Leiomyosarcoma of the Nasopharynx. Glen D. Dobben. Arch. Otolaryng. **68:** 211–213, August 1958. (Henry Ford Hospital, Detroit 2, Mich.)

A search of the literature disclosed no record of a leiomyosarcoma of the nasopharynx. The author reports a case in a 69-year-old woman whose presenting complaint was difficulty in breathing through her left nostril for one year. There was some associated stuffiness in the left ear, with pain along the left side of the throat. On physical examination a whitish-gray tumor could be seen on the floor of the left nasal choana beneath the inferior turbinate posteriorly. Roentgenography also showed a 3 × 2 × 2 cm. soft-tissue mass obstructing the left posterior choana, with its origin in the posterior portion of the left inferior turbinate. The turbinate was not destroyed, but the medial aspect of the bone was less distinct than the opposite site. The location of the tumor was clearly delineated by the surrounding air. It was impossible roentgenologically to say whether it was benign or malignant. A soft-tissue mass of this size in a posterior location is more apt to be malignant. The benign nasopharyngeal fibroma usually originates more superiorly and in the anterior part of the nasopharynx.

Biopsy findings were inconclusive, and the tumor was therefore excised with a surgical snare under a local anesthetic. The final diagnosis was leiomyosarcoma. The residual tumor was later electrocoagulated under general anesthesia. After one year there was no evidence of recurrence.

Two roentgenograms; 1 photomicrograph.

Radiological Aspects of New Growths of the Larynx. Satyen Basu. Indian J. Radiol. **12:** 89–93, May 1958. (Chittaranjan Cancer Hospital, Calcutta, India)

The findings on plain lateral roentgenograms of the neck in carcinoma of the larynx are presented and correlated with the indirect laryngoscopic findings in the same cases. Various abnormal shadows produced by the neoplasms are described in the text, but are not very clearly shown in the accompanying roentgenograms. The value of roentgenograms of the soft tissues in showing the extension of the tumor is emphasized, particularly its downward extent in the lower hypopharynx.

Twelve roentgenograms.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

Early Diagnostic Criteria of Congenital Hypothyroidism: A Comprehensive Study of Forty-Nine Cretins. George H. Lowrey, Richard H. Aster, Edward A. Carr, Govind Ramon, William H. Beierwaltes, and Norma R. Spafford. J. Dis. Child. **96:** 131–143, August 1958. (University Hospital, Ann Arbor, Mich.)

A group of 49 cretins was studied at the University Hospital, Ann Arbor, Mich., in an attempt to find as many criteria as possible that might lead to an early diagnosis. All the patients were followed for periods of one to over thirty years. All were white, and the age range was from twelve months to thirty-two years.

Diagnosis of cretinism can usually be made before the infant is three months old and certainly before six months of age, with the aid of a careful history, adequate physical examination, and a few laboratory procedures. The most commonly observed findings, in order of frequency, were: lethargy, constipation, feeding problems (slow and uninterested feeding, choking, and failure to gain weight), respiratory difficulties, umbilical hernia, and skin changes. Three or more of these were present in over 50 per cent of the patients by the end of the first month and in 75 per cent of the patients by the end of the third month of life.

Estimation of the serum protein-bound iodine or butanol-extractable iodine is the most valuable laboratory test in establishing diagnosis because of its reliability and the fact that exposure to radioactivity is avoided. This last factor is the only serious limitation to measuring the I^{131}-uptake by the thyroid, an equally reliable diagnostic procedure. In goitrous patients and possibly in a small number of others, more exact identification of iodinated compounds in the blood is required, and additional laboratory studies may be necessary.

The evaluation of bone maturation is a valuable screening device. Delay in appearance of epiphyseal centers is not specific for hypothyroidism, and the diagnosis cannot be confirmed solely on this basis, but absence of delay is extremely strong evidence against cretinism. In every patient in this series who was given an adequate roentgen examination, easily measured retardation was present.

One chart; 3 tables.

THE CHEST

Carcinoma of the Lung. Practical Classification for Early Diagnosis and Surgical Treatment. Lyman A. Brewer, III, Angel F. Bai, John N. Little, and Gregorio Rabago y Pardo. J.A.M.A. **166:** 1149–1154, March 8, 1958. (L. A. B., 2010 Wilshire Blvd., Los Angeles 57, Calif.)

The authors present a practical classification of bronchogenic carcinoma based on a study of 489 patients, of whom 291 were subjected to thoracotomy. The cases are classified according to the area of occurrence: (1) main bronchus; (2) lobar bronchus; (3) mid-lung; (4) subpleural. The tumor occurred in a main bronchus in 71 (24 per cent) of the present series, in a lobar bronchus in 156 (54 per cent), in a midlung zone in 31 (11 per cent), and in a subpleural location in 33 (11 per cent). Bronchoscopy offers the most satisfactory means of positive diagnosis in the main bronchus location and 54 per cent of the lobar bronchus carcinomas were visualized by this means. The mid-lung and subpleural carcinomas were beyond the limits of bronchoscopic visibility. In one-fourth of the cases presented, it was possible to

obtain a positive biopsy at bronchoscopy. Smears of the sputum stained for cancer cells were helpful in a relatively small percentage of cases.

In those patients subjected to thoracotomy, the midlung carcinomas were the most favorable for resection, which was possible in 94 per cent. The neoplasms of the main bronchus and lobar bronchus were the next most favorable groups, showing 69 and 61 per cent resectability. The subpleural group was the least favorable, only 42 per cent being resectable. The authors feel that the high percentage of resectability for the midlung field lesions is important to the radiologist, since the diagnosis is dependent on the demonstration of a suspicious shadow on the chest roentgenogram. Bronchoscopy and stained sputum smears are almost always negative in these cases.

Operative mortalities were about the same in the four groups, but early results indicate an 84 per cent survival one year after surgery in the midlung group. This is believed to be due to the fact that fewer lymph node metastases were seen in this group. The midlung group also displayed the highest proportion of asymptomatic cases and those with symptoms had had them for a shorter interval. No significant age difference was noted between the four groups.

The "negative" chest films from previous examinations, when compared to films under consideration, supply the key information in making an early diagnosis of lung cancer. For this reason, the film should be considered of the utmost value and, if storage facilities are not available to the radiologist, the patient, himself, should be allowed to keep such studies.

Two roentgenograms; 4 drawings; 2 tables.

NORMAN L. ARNETT, M.D.
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Radiological Diagnosis of Primary Lung Tumors. N. G. Gadekar. Indian J. Radiol. **12:** 74–88, May 1958. (All-India Institute of Medical Science, Safdarjang, New Delhi 3, India)

The author divides the roentgen findings in carcinoma of the lung into several general groups. The first two general catagories consist of opacification of an entire hemithorax with shift of the mediastinum either away from the opacity or toward the lesion. A brief discussion of the roentgen picture in atelectasis is presented. The other general groups of findings discussed are large homogeneous shadows, single and multiple shadows, and cavitary lesions. Tomographic and bronchographic observations are briefly recorded. Reproduction of the roentgenograms is not very satisfactory, and one has considerable difficulty visualizing some of the findings described.

The author emphasizes the value of attempting to describe the pathophysiologic change which the tumor has caused in the lung on the basis of the shadow produced in the roentgenogram.

Thirty-eight roentgenograms.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

Uncommon Roentgen Patterns of Pulmonary Sarcoidosis. Benjamin Felson. Dis. of Chest **34:** 357–367, October 1958. (Cincinnati General Hospital, Cincinnati, Ohio)

This report deals with some of the less familiar roentgen patterns of pulmonary sarcoidosis, namely, the multinodular and the multicystic forms.

In cases of the multinodular type the roentgen changes are far out of proportion to the mild clinical manifestations. There are numerous round or oval lesions, 5 to 40 mm. in diameter, widely distributed in the lungs. In 4 of 5 cases studied by the author the nodules appeared to be more numerous in the central zones, where they tended to be confluent. The individual nodules in these 4 cases presented a hazy or fluffy outline, the "soft" margin sometimes appearing as a halo around the central density. The confluence of the nodules and their lack of sharp borders did not closely simulate the common type of metastases, but the resemblance to the "halo" nodules of chorionepithelioma, also seen occasionally with other metastatic tumors, was striking. In 3 of the cases the superior mediastinum appeared widened, presumably due to lymph node enlargement.

Certain features encountered in this group of cases should provide the clue to the correct diagnosis. These include the mild symptoms and the continued well-being of the patients; the presence in other body systems of stigmata consistent with sarcoidosis, especially lymphadenopathy; the apparent predilection for young Negroes; the fluffy margins of the pulmonary nodules and their tendency to become confluent; and the stationary or even regressive course shown roentgenographically.

The multicystic pattern of sarcoidosis, of which 9 examples were seen, is probably a complication of the irreversible fibrotic stage of the disease. It is not infrequently encountered at autopsy in patients dying of sarcoidosis but has seldom been emphasized as a prominent or predominant roentgen manifestation of the disease. On the initial roentgenogram multicystic lesions were the predominant feature in a single case, although they were present to some degree in several others. In the remaining 8, extensive pulmonary infiltrate was apparent, fibrotic in nature in 6 and miliary in 2. In 2 cases, 1 with fibrosis and 1 with miliary densities, the involvement was limited to one lung. The unilateral miliary lesions exemplified an exceedingly rare distribution of this form of sarcoidosis. Mediastinal and/or hilar enlargement was evident on the first film in 7 cases and appeared later in 1. Spontaneous pneumothorax occurred terminally in 1 case.

In following the progression of the lesions the ultimate appearance was often quite characteristic. There was widespread involvement of the lungs with strand-like or ill-defined densities honeycombed with large or small thin-walled cavities having the typical appearance of bullae in 7 cases and of cystic bronchiectasis in 2. In addition—and an important part of the picture—there was definite enlargement of the hili and/or the superior mediastinum. The margins of the broadened mediastinum lacked the usual sharp definition seen in the earlier stages of sarcoidosis because the adjacent pulmonary lesions overlapped and obscured them to some degree.

In the differential diagnosis any condition which causes widespread pulmonary fibrosis and which results in bullous emphysema or cystic bronchiectasis, must receive consideration. Many diseases fall into this category, including tuberculosis, histoplasmosis, diffuse interstitial fibrosis of Hamman and Rich, scleroderma, bronchiectasis, progressive bullous emphysema or "vanishing lung," pneumoconiosis, and the later stages of chronic bronchial asthma. The enlarged

tracheobronchial nodes and earlier chest roentgenograms showing the more typical appearance of sarcoid, as well as the presence of other clinical and laboratory evidence consistent with sarcoidosis, suggested the correct diagnosis.

The seriousness of the multicystic form of pulmonary sarcoidosis is evident when it is pointed out that 5 of the 9 patients described here died and that 2 others were doing poorly when last seen.

Nine roentgenograms. THEODORE E. KEATS, M.D.
University of Missouri

Concerning the Roentgen Diagnosis of Pulmonary Edema. G. Herrnheiser. Fortschr. a. d. Geb. d. Röntgenstrahlen **89:** 125–135, August 1958. (In German)

Classical signs of pulmonary edema are: (1) bilateral central location with predominantly symmetric arrangement, (2) clear peripheral and paramediastinal zones, and (3) a narrow "waist," resulting in a butterfly pattern. Numerous variations such as unilateral involvement, lack of symmetry, and atypical location exist. The peripheral zones, the superior mediastinum, and the "waist," however, always remain clear, as corroborated by lateral and oblique views of the chest.

While most pulmonary lesions follow a distribution pattern according to pulmonary segments, the distribution of edema is reminiscent of the division of lobes postulated many years ago by Felix. According to that author, each lobe can be subdivided into a root, a central, and a peripheral zone. Some pathologic processes may develop only in the periphery, while others are localized mainly in the central zone and root. These observations suggest a functional difference of the zones. The characteristic appearance of pulmonary edema can be explained only on the basis of a predominantly central location.

Numerous roentgenograms illustrate typical and atypical appearances, as well as the course of pulmonary edema. Photographs of specimens serve to explain the author's concept of the different zones of pulmonary lobes. ERNEST KRAFT, M.D.
Northport, N. Y.

Chronic Pulmonary Insufficiency Secondary to Silo-Filler's Disease. Gilbert M. P. Leib, W. N. Davis, Trave Brown, and Mark McQuiggan. Am. J. Med. **24:** 471–474, March 1958. (W. N. D., Inkster, Mich.)

The clinical syndrome produced by acute toxicity from exposure to the oxides of nitrogen (primarily nitrogen dioxide) consists, briefly, of dyspnea, weakness and cough, associated with a choking sensation or inability to breathe deeply, occurring during or immediately after exposure to silage gas. Several victims have seen a yellow-to-brown or red colored gas which had collected above the silage. A latent interval of two to three weeks was noted in some cases, during which time the symptoms remained stationary or were but slightly progressive. Following this interval, chills, fever, increasing dyspnea, and cyanosis occurred, leading to death within three and a half to six weeks. Autopsy studies have disclosed pulmonary edema and bronchopneumonia in those patients dying within a few days of exposure, and bronchiolitis fibrosa obliterans in patients dying after three to four weeks. Chest roentgenograms may show patchy areas of pneumonitis or multiple granular to nodular densities in the lung fields which gradually resolve in those patients who recover.

The authors present a case which they believe to be the first recorded in which chronic pulmonary disease ensued as a result of exposure to silage gas. They first saw the patient in 1957, when he complained of "smothering and headaches" about two and a half years after working in a recently filled silo for approximately five minutes. He had become ill immediately after exposure to the gas, with what was diagnosed as "flu." A chest roentgenogram was reported as "negative." The acute episode lasted for three weeks. In December 1955, the patient was admitted to a sanitarium as a tuberculosis suspect, but was discharged within a few weeks with a diagnosis of bronchopneumonia.

The patient was a well developed, well nourished white man in moderate respiratory distress with slight peripheral cyanosis. The temperature was 102° F., respiratory rate, 25 per minute, pulse rate 100. The chest was symmetrical, with equal expansion bilaterally. Inspiratory and expiratory moist râles and scattered expiratory wheezes were heard throughout both lung fields; vocal and tactile fremitus as well as percussion note were normal. There was no clubbing of the fingers. A chest roentgenogram revealed accentuation of the bronchovascular markings in the upper portions of both lung fields, but there was no evidence of active parenchymal disease. Pulmonary function studies on the second hospital day showed a vital capacity of 1,450 c.c., 36.2 per cent of the predicted normal value. Maximum breathing capacity was 17 per cent of normal. In three seconds the patient could exhale 69 per cent of his vital capacity.

While such a disparity between the minimal chest x-ray findings and the markedly impaired pulmonary function is at first surprising, it might be expected in a diffuse process primarily affecting the bronchioles of the lung. In addition, the finding of markedly diminished maximum breathing capacity, disproportionately depressed in comparison to the vital capacity, and extremely slow expiratory effort, reflected by the timed vital capacity, point to diffuse bronchiolar disease.

Some improvement followed the administration of expectorants and antimicrobials and bronchodilatation with intermittent positive pressure. It was apparent in this case, however, that a severe degree of residual impairment in pulmonary function existed and was not reversible.

One roentgenogram; 2 vital capacity curves; 1 table.

Pulmonary Actinomycosis. Thomas A. Warthin and Boris Bushueff. Arch. Int. Med. **101:** 239–243, February 1958. (VA Hospital, West Roxbury, Mass.)

Three typical cases of pulmonary actinomycosis without significant pleural or thoracic wall involvement are reported. The diagnosis in these cases was established by culture and operation. Two of the patients were admitted to the hospital with a presumptive diagnosis of cancer of the lung. Adequate fungus studies were made in only 1 patient; had they been performed in the other 2, the correct diagnosis probably would have been made without surgery.

The roentgen findings in these 3 cases of pulmonary actinomycosis had a certain common denominator

which, in the authors' opinion, is significant enough to enter into the differential diagnosis of pulmonary lesions. This consists of a fan-shaped or lobulated consolidation near the hilus, or radiating from it, usually posterior, frequently involving an apical segment of a lower lobe. This may not be easily differentiated from the usual appearance of neoplasm or pneumonia. Secondary lesions are occasionally present in other portions of the lung.

It is recommended that in patients in whom carcinoma is suspected, with central hilar involvement radiating into the periphery of the lung and with suggestive lymph node enlargement, careful smear and culture of the sputum for Actinomyces be carried out prior to surgery.

Six roentgenograms.

The So-Called Aspergilloma. A. Brunner. Schweiz. med. Wchnschr. **88**: 559–563, June 7, 1958. (In German) (Chirurgische Universitätsklinik Zürich, Switzerland)

Six cases of pulmonary aspergilloma which the author describes as a lung cyst filled with the fungus are reported. The clinical picture is often characteristic, with hemoptysis recurring over a period of years. Roentgen studies show a typical round or oval density surrounded by a circle or crescent of air at the upper pole. While this "air sickle" is characteristic, it is not entirely pathognomonic, since it may also be produced by tuberculoma. Aspergilloma usually occurs in the upper lobes. The diagnosis can often be confirmed by demonstration of the fungus in the sputum. Therapy consists of surgical removal of the lesion.

Nine roentgenograms; 1 photomicrograph; 4 photographs. JULIUS HEYDEMANN, M.D.
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Concerning Postpneumonic Pseudo Air Cysts in Children. K. Schlager. Fortschr. a. d. Geb. d. Röntgenstrahlen **89**: 136–146, August 1958. (In German) (Wilhelminenspital, Vienna, Austria)

Postpneumonic air cysts in children have become widely recognized, especially since the introduction of modern chemotherapy and antibiotic medication. In the literature the cysts are also known as tension cysts, valve cysts, localized bullous emphysema, metapneumonic emphysema, pneumatocele, pseudocavity, absorption-ring formation, acquired cysts, obstructive emphysema, etc. These pseudo air cysts are characterized by marked change in size, pressure displacement of the mediastinum, lack of symptoms, and spontaneous regression even without therapy. They are believed to be due to a check-valve mechanism of small bronchi or to poststenotic distention of a suppurating process.

The diagnosis is based on the history of pneumonia and the roentgen demonstration of round or ovoid ring formations with a thin wall. Fluid levels are absent in the majority of cases. When the cyst appears smaller than the original lesion, it is possibly due to a clearing abscess; when it is larger, a poststenotic air distention is the most likely cause. Bronchography, bronchoscopy, and tomography are difficult to perform in children and usually are not indicated.

In the differential diagnosis the following conditions have to be considered: postpneumonic abscess, partial pneumothorax and tension pneumothorax, pneumonitis with bronchiectasis, congenital cysts of the lung (very rare and permanent, without change in size), diaphragmatic hernia, tuberculous cavity, and ring formation due to Echinococcus, dermoid cyst, or neoplasm.

Four cases are reported and illustrated. In 3 of these complete clearing ensued within a period of a few weeks. In the fourth case significant regression was noted only after a lapse of eight months.

Fourteen roentgenograms. ERNEST KRAFT, M.D.
Northport, N. Y.

Varicella Pneumonia with Prolonged Roentgenologic Change. Allen G. Brailey, Jr., and Kjeld O. Husebye. Minnesota Med. **41**: 695–698, October 1958. (K. O. H., 350 St. Peter St., St. Paul 2, Minn.)

The clinical features of 57 cases of varicella pneumonia reported since 1942 and 3 additional cases observed by the authors are reviewed in this article. Roentgen examination revealed diffuse miliary infiltration with coalescent areas spreading from the hilar regions into the lower lung fields. The pulmonary infiltration was followed in 19 cases to complete resolution, 12 patients were lost to follow-up, 7 died, and 19 cases were not reported on.

The first of the authors' 3 cases was an example of zoster-varicella virus pneumonia in a 67-year-old man with chronic lymphatic leukemia and the cutaneous manifestations of generalized herpes zoster. In the second and third patients, a 37-year-old man and a 55-year-old woman, both of whom were treated with ACTH and broad spectrum antibiotics, miliary pulmonary infiltration persisted on roentgenograms of the chest taken fifteen months after the acute illness. This persistence suggests the possibility of a relationship to the use of ACTH during the acute attack or to previously administered adrenocortical hormones. If this were the case, then increased invasiveness or persistence of virus in the tissues during steroid medication, as has been observed in certain experimental bacterial infections, is a possible mechanism by which the steroids could have enhanced development of more severe infiltration. The authors believe it more likely that the administration of ACTH reversed the toxic picture in patients who otherwise would have succumbed to their disease, and the present roentgen picture reflects the seriousness of the acute phase.

The administration of prednisolone after amelioration of the acute symptoms did not appreciably affect the resolution of the diffuse pulmonary infiltration.

Three roentgenograms.

A Large Pseudoaneurysm Caused by Extrapleural Plastic Ball Plombage. Masashichi Kawano, Soroku Saheki, and Yuzaburo Murata. Dis. of Chest **34**: 222–225, August 1958. (Nagasaki University School of Medicine, Nagasaki, Japan)

The most common complication of plastic plombage as a means of collapse therapy for pulmonary tuberculosis has been the perforation of the cavity wall and subsequent empyema. Little attention has been given to the danger of perforation of important intrathoracic vessels.

The authors report a case of pseudoaneurysm in a 32-year-old man nearly seven years after introduction of several large plastic balls for a tuberculous lesion of the left upper lobe. Because of profuse hemorrhage a thoracotomy was performed. The lower lobe was found to be almost intact but the upper lobe was compressed to the wall by pressure from inside. Ar-

terial blood filled the chest upon removal of the first ball to be found and the other floating balls were then promptly removed, gauze packing was placed in the chest, and the wound was closed. At repeat surgery a week later, massive arterial bleeding again occurred. The patient was then sent to the Department of Radiology for angiographic studies.

Fifty cubic centimeters of 76 per cent Urografin was injected through the right saphenous vein. An unusual finding in the vault of the left thorax was a round or oval homogeneous shadow of clear smooth outline which spread from the upper border of the second rib to the fourth rib. This was thought to be a large aneurysm communicating with the left subclavian or common carotid artery. Unfortunately a lateral angiogram was not obtained.

Three days later the patient died suddenly. At autopsy, a large sac communicating with the subclavian artery was found. This was filled with blood and lined with fibrinous membrane of many layers without any vessel wall structure. Apparently this was a pseudoaneurysm formed by repetition of the bleeding and coagulation process.

Clinical and postmortem findings made it clear that the round edge of the plastic ball adjacent to the subclavian artery gave continuous pressure against the vessel wall for nearly seven years and finally perforated it. High arterial pressure did not allow the closure of the perforation and bleeding was repeated. This led to a high pressure in the collapsed space which was in contact with the pathologic lung surface with resultant preoperative pulmonary hemorrhage through the bronchial route. Atfer successful removal of the upper lobe at the second operation, the bleeding finally pressed into the already infected bronchial stump. This gave way to flow of blood into the trachea with consequent asphyxia.

The authors believe plastic plombage as treatment in pulmonary tuberculosis is inadvisable except in a few selected cases. To safeguard against severe complications they advocate the substitution of pulmonary resection or thoracoplasty.

Three roentgenograms.

Complete Intrathoracic Goiter Simulating an Aneurysm of the Ascending Aorta. Report of a Case. John B. Codington and R. Adams Cowley. J.A.M.A. **167**: 461–463, May 24, 1958. (University of Maryland School of Medicine, Baltimore, Md.)

A case of complete intrathoracic goiter without visible connection with the neck is presented and the literature is reviewed. Only 7 similar cases have been recorded, indicating the rarity of the condition. The most common location of anomalous thyroid tissue is within the thorax. Two general groups of cases are recognized: (1) aberrant mediastinal goiter and (2) substernal goiter. The case reported falls into the first group arising from aberrant mediastinal thyroid tissue having no connection with the thyroid gland proper.

The problem of differentiation between various thoracic lesions and complete intrathoracic goiter becomes extremely difficult because of conflicting results in diagnostic studies. In this case angiocardiography demonstrated extreme vascularity of the tumor, leading to the diagnostic impression of a small saccular aneurysm. A radioactive iodine survey suggested a substernal or mediastinal thyroid mass. The diagnosis was established at operation and the aberrant mass was removed.

Two roentgenograms; 1 photomicrograph.

NORMAN L. ARNETT, M.D.
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Aseptic Cavitation of Pseudotumors in Anthracosilicosis: Clinical and Radiological Study. J. Prignot and R. Van de Velde. J. franç. de méd. et chir. thorac. **12**: 623–645, 1958. (In French) (Université de Louvain, Belgium)

The authors describe aseptic cavitation in 22 of 600 miners with confluent or massive anthracosilicosis. Most of these patients had been exposed for several years to the irritant dusts. At first the walls of the cavities seem irregular and rather thick but later become very thin. The cavities rarely undergo occlusion by retraction.

Laboratory studies are important in ruling out tuberculosis. It is possible that an old tuberculous focus might be activated by an aseptic necrosis of the nature described in this paper.

Eight roentgenograms; 1 graph.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

THE HEART AND BLOOD VESSELS

Evaluation of Conventional Roentgenologic Methods in the Study of Congenital Heart Disease. Charles W. Vickers and Owings W. Kincaid. Minnesota Med. **41**: 680–686, October 1958. (Mayo Clinic, Rochester, Minn.)

In about 80 per cent of patients with congenital cardiac disease, an accurate determination of the type of malformation and an adequate prediction of the result of operation can be made by correlation of the clinical history, physical examination, electrocardiographic evidence, and conventional roentgen studies of the chest. In the remaining 20 per cent the necessary information may be obtained by cardiac catheterization (in about 10 per cent) and by angiocardiography (10 per cent).

A large group of cardiac anomalies may be considered together since the hemodynamic alterations are similar in that they are characterized by an arteriovenous or left-to-right shunt and therefore have similar roentgenologic features. This group includes ventricular septal defect, atrial septal defect, patent ductus arteriosus, persistent common atrioventricular canal, and anomalous pulmonary venous connection. The roentgen characteristic of these malformations is an increase in the size of the main pulmonary artery and its central and peripheral branches as evidence of increased flow in the pulmonary artery.

The other large group of cardiac anomalies that have gained importance since they are now surgically correctable are those that are characterized by varying degrees of pulmonary stenosis. The most common of these are pulmonary stenosis with ventricular septal defect or tetralogy of Fallot, and isolated pulmonary stenosis, which may or may not be associated with atrial septal defect. The *coeur-en-sabot* configuration is usually said to be characteristic of tetralogy of Fallot. This has been noted, however, in only about 20 per cent of patients with tetralogy, and its absence by no means precludes the diagnosis. A right-sided aortic arch is more commonly associated with tetralogy

than with other cardiac anomalies, being present in about 25 per cent of these patients.

The most suggestive sign of isolated pulmonary stenosis is poststenotic dilatation of the pulmonary artery. This may be the only roentgen sign of abnormality. Not infrequently the left pulmonary artery also may be enlarged and found to pulsate vigorously, while the right pulmonary artery is normal.

Bing (Ann. Int. Med. **37**: 664, 1952) has stated that "roentgenographic examination constitutes the most important part of the clinical examination in congenital heart disease." This statement, not by a radiologist but by one who has made important contributions to knowledge of cardiac physiology, constitutes an unbiased opinion of the potential importance of the radiologic examination. The extent to which this potential is realized is dependent on the radiologist's knowledge of the basic pathology, clinical and physiologic aspects of cardiac disease, and his ability to integrate this knowledge with the roentgenologic findings in a given case.

Ten roentgenograms; 4 diagrams.

Pulmonary Hypertension in Congenital Heart Disease. William Evans and D. S. Short. Brit. Heart J. **20**: 529–551, October 1958. (London Hospital, London, England)

Basically this is a study of the microscopic changes in the pulmonary vasculature in 11 cases of shunts with pulmonary hypertension (3 atrial septal defects, 3 ventricular septal defects, 4 patent ducti, and 1 aortopulmonary septal defect). Pulmonary hypertension is defined as persistent elevation of pulmonary blood pressure causing enlargement and ultimate failure of the right ventricle with characteristic clinical, radiological, and electrocardiographic findings.

The findings varied with the nature of the congenital defect, though the pulmonary artery changes were uniform, differing in no important respect from those observed in solitary pulmonary hypertension or in hypertension associated with mitral stenosis. In the presence of an *atrial septal defect* radiology will reveal great enlargement of the pulmonary artery and its primary branches, which on fluoroscopy are seen to pulsate excessively unless occluded by thrombus, as sometimes happens. The periphery of the lung fields is clear. There is considerable enlargement of the right atrium and ventricle. The aortic knuckle is either small or hidden by the distended pulmonary artery.

In their cases with a *ventricular septal defect*, the authors observed moderate enlargement of the heart and enlargement of the pulmonary arterial trunk and its main branches similar to or greater than that in the cases with atrial septal defects.

With a *patent ductus arteriosus* the heart, as a rule, is only moderately enlarged, but the pulmonary trunk and its main branches may be considerably dilated and show exaggerated pulsation. The periphery of the lung fields tends to be abnormally translucent.

The authors do not describe the radiologic findings in their single case of *aortopulmonary trunk*. They quote others as having reported right ventricular hypertrophy and a thickened ventricular wall.

Among the clinical findings, which also vary with the type of defect, are: dyspnea, cyanosis, cardiac pain, fainting, small pulse, peripheral edema, hemoptysis, and pulmonary infarction.

Histologic examination (also postmortem pulmonary arteriograms) showed widespread occlusion of smaller arteries and arterioles with patchy intimal thickening in vessels not completely occluded. Development of pulmonary hypertension did not appear to be related to the size of the shunt or the age of the patient but possibly to some inherent predisposition. Once well established pulmonary hypertension would contraindicate surgical attempts to close the shunt. In younger patients temporary closure may be tried and, if pulmonary pressure does not rise and the aortic pressure does not fall, then the shunt may be closed.

Eight roentgenograms; 19 photomicrographs; 8 electrocardiograms.

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Congenital Absence of a Main Branch of the Pulmonary Artery. Report of Three New Cases Associated Respectively with Bronchiectasis, Atrial Septal Defect and Eisenmenger's Complex. Israel Steinberg. Am. J. Med. **24**: 559–567, April 1958. (New York Hospital-Cornell Medical Center, New York, N. Y.)

Congenital absence of a main branch of the pulmonary artery may be an isolated abnormality or associated with septal defects. Unless there is bronchiectasis in the lung without a pulmonary artery, patients in the first group are usually asymptomatic. Pulmonary function and hemodynamic studies in this group are usually within the normal range, even though oxygen uptake on the involved side is negligible. Diagnosis may often be made by inspection of the conventional roentgenogram, which shows a hypoplastic, poorly vascularized lung on one side with a fully vascularized, distended opposite lung that causes mediastinal herniation. Diagnosis in the cases with associated cardiac septal defects is more difficult. The patients are often ill, with recurrent infections, dyspnea, and cyanosis.

Angiocardiography provides the definitive diagnosis of absence of a pulmonary artery main branch. Cardiac catheterization may be needed to establish the level of a cardiac shunt, whether atrial or ventricular; in the latter, it is also necessary to differentiate between the tetralogy of Fallot and the Eisenmenger complex. Angiocardiography also provides information regarding the systemic circulation in the lung with the missing artery. Indirect evidence of bronchial arterial circulation can be demonstrated by the circulatory pattern following aortic opacification; ascending aortic pulmonary arterial branches, if present, can readily be recognized. Differentiation of the isolated from the complicated types of absence of a pulmonary artery is significant because of therapeutic and prognostic implications.

Three cases are reported. In 1 case isolated absence of the right pulmonary artery was associated with cystic bronchiectasis of the same lung. Lack of significant pulmonary fibrosis in the right lung in this case makes it unlikely that the absence of the right pulmonary artery was secondary to the bronchiectasis. In the second, an atrial septal defect was associated with absence of the left pulmonary artery. The last case, with absence of the right pulmonary artery, was associated with Eisenmenger complex, and a right pulmonary artery arising from the ascending aorta was noted.

Sixteen roentgenograms.

Congenital Atresia of the Inferior Vena Cava, Common Iliac Veins, and Left Innominate Vein: A Case with Extensive Development of Superficial Venous Collateral Circulation. Kenneth F. Swaiman, Sol Austrian, and Richard B. Raile. J. Dis. Child. **96:** 81–86, July 1958. (University of Minnesota Medical School, Minneapolis 14, Minn.)

A case is reported of a newborn Negro boy with extensive superficial venous collateral circulation involving the abdomen, chest, back, neck, and posterior head. Angiograms demonstrated an apparent atresia of the postrenal segment of the inferior vena cava, the common iliac veins, and the left innominate vein. These defects are believed to have stemmed from maldevelopment of the right supracardinal vein and also of the precardinal anastomosis, both of which are formed sometime during the seventh week of gestation.

The patient was in good health at one year of age, but it is thought that the superficial exposure of the anomalous veins makes traumatic rupture or laceration a potential threat to life. In addition, as the patient grows older and assumes an upright position, the lack of valves will permit massive pooling of blood in the vessels of the legs and lower trunk, with probable formation of varicosities and edema.

Congenital atresia of the inferior vena cava appears to be well documented in only one previous case (Edwards and Bennett: J. Pediat. **51:** 453, 1957. Abst. in Radiology **71:** 286, 1958).

Four roentgenograms; 1 photograph; 3 drawings.

Congenital Arteriovenous Aneurysms. F. S. Cross, D. M. Glover, F. A. Simeone, and F. A. Oldenburg. Ann. Surg. **148:** 649–663, October 1958. (St. Luke's Hospital, Cleveland, Ohio)

This paper is primarily a discussion of the problems presented by arteriovenous aneurysms and methods for their treatment. Eight cases are reported in moderate detail.

Methods for investigation of abnormal vascular communications include arteriography and various other forms of angiography. It appears that cineangiography is most likely to provide the surgeon with helpful information by allowing identification of arterial and venous phases of the shunting process and localizing more accurately the region of the arteriovenous anastomosis. Angiograms in general are helpful in providing information on size and extent of lesions and their collaterals and ramifications. Congenital arteriovenous aneurysms tend to present multiple vascular shunts, often with additional tiny channels not readily appreciated.

The authors stress the fallacy of ligating major arteries which feed local lesions without resecting the arteriovenous communications. Such a course of action, especially in lesions of the extremities, may lead paradoxically to massive thrombosis of venous channels, unbearable pain, and increased bleeding from existing areas of ulceration.

Histologic studies show that the larger arteries tend to undergo thrombosis, revascularization by many thin-walled vessels, and interlacing fibroblasts. This series of events produces a picture sometimes difficult to differentiate from frank neoplasia.

Eighteen illustrations including 9 roentgenograms; 4 tables.

JAMES W. BARBER, M.D.
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Congenital Aneurysm of the Coronary Artery with an Arteriovenous Fistula. Troels Munkner, Olaf Petersen, and Jörgen Vesterdal. Acta radiol. **50:** 333–340, October 1958. (University Hospital, Copenhagen, Denmark)

A congenital aneurysm of the coronary artery with an arteriovenous fistula was demonstrated by thoracic aortography in a 6-year-old boy. At the age of two and a half years, a continuous murmur was heard over the heart but no other signs of heart disease were present. Chest films revealed a prominent main pulmonary artery, slightly increased pulmonary vascularity, and questionable left ventricular enlargement. At six years, the patient was admitted to the hospital, relatively asymptomatic, for further evaluation. There had been no cyanosis. A continuous murmur was again present but seemed superficial, resembling the murmur present in an arteriovenous fistula involving the internal mammary artery and vein. An electrocardiogram was normal and chest films showed no change in the cardiovascular silhouette.

Cardiac catheterization revealed a slight shunt from the left side to the right ventricle, with one sample from the apex of the right ventricle showing an oxygen saturation of 87 per cent. On the basis of these findings, a small ventricular septal defect was thought to be present. Subsequent angiocardiography showed slight refilling of the right ventricle.

The peculiar character of the murmur led to thoracic aortography, which demonstrated a dilated left coronary artery ending in a spherical aneurysm measuring 1.5 × 1.5 cm. This aneurysm communicated with an irregular cavity in the anterior right ventricular wall, and in a later phase of the aortogram, contrast medium entered the right ventricle from the cavity in the wall at the very site where catheterization had revealed a sample with elevated oxygen saturation.

Since the patient was relatively asymptomatic, the shunt was small, and normal pressures were found at catheterization, surgery was not performed. Should subsequent catheterization show an essentially increased shunt, the question of operation may be reconsidered.

Five roentgenograms; 1 table.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

Coarctation of the Aorta: Aortographic Studies Before and After Operation. Bror Brodén and Johan Karnell. Acta radiol. Suppl. 165, 1958. (Södersjukhuset, Stockholm, Sweden)

In the years 1948 to 1956 the authors investigated 123 cases of coarctation of the aorta. In 115 of these aortography was performed; in the remaining 8 (in children) angiocardiography was used with injection of the medium into the pulmonary artery. The patients ranged in age from four to fifty years. Males predominated over females 2.5 to 1.

A classification of typical cases based on the appearance of the prestenotic segment has proved useful. In Type I the distal part of the aortic arch is fairly long and wide; in Type II, fairly long but narrow; in Type III, short; in Type IV, atresic. Atypical cases form a fifth group.

Moderate stenosis was rare in the authors' material, the constriction being usually complete or extreme. The poststenotic segment was in most instances dilated. A patent ductus arteriosus is a commonly associated lesion. In the majority of cases the patent

ductus is narrow and of no hemodynamic consequence. In 5 cases in this series it was wide enough to be identified on aortography. The left subclavian often appears as a direct continuation of the aortic arch and is of the same width. The width of the arch is dependent upon the extent to which the left subclavian functions as a collateral.

Aortic incompetence is the most commonly associated lesion in coarctation of the aorta. In most of the authors' cases the incompetence was mild. In their severe cases the ascending aorta was not markedly dilated; on the aortogram regurgitation to a distinctly dilated left ventricle was apparent. This often makes it difficult to demonstrate the stenosed region, since repeated regurgitation causes dilution of the contrast medium.

Only 4 in this series of cases are classed as atypical: 3 cases in which the constriction was proximal to the origin of the left subclavian and 1 case with multiple moderate stenoses of the aortic arch and descending aorta, with intermediate aneurysms.

In the typical cases of coarctation, the collateral circuit was symmetrical. If stenosis was not complete or extreme, the collateral circuit was poorly developed or was lacking. The collateral vessels are thin-walled and show a tendency to aneurysm and arteriosclerosis. Narrow collaterals in an adult with coarctation indicate that stenosis is not complete but are not an unquestionably favorable sign.

Postoperative roentgen studies were made in 105 cases and in 82 cases the minimum width of the anastomosis was compared with both the width of the aorta proximal to the stenosis and with the body surface. In each patient the anastomosis was measured in two planes.

The appearance of the anastomosis varied from case to case due to anatomical differences and to the method of suturing, but anastomoses of varying width were obtained with both the anatomic and everting technics.

The ratio of the width of the anastomosis to that of the proximal aorta is designated as Index I. This was normal in 9 patients; in a few, it exceeded 1 but in the majority was between 0.25 and 0.70. In 7 cases the area of the anastomosis was less than one-fourth that of the aortic arch. Index II, based on the ratio of the diameter of the anastomosis to the body surface, indicated that in the majority of cases the lumen was smaller at the anastomotic site than that of a normal aorta.

A collateral circuit persisting after operation can be demonstrated by aortography. When the collateral circulation has diminished or lessened, some of the earlier collateral vessels become filled with contrast medium. Filling takes place slowly, and reaches a maximum after the greater proportion of the medium has passed through the anastomosis. If the blood flow has changed its direction in the first pair of posterior intercostal arteries as well, this is a criterion of cessation of the collateral circulation.

Four patients with follow-up of five years were operated on during the period of growth. In two of these patients aortograms were taken twice after operation. There was "proof" that the anastomosis grew with the aorta.

Sixty-two roentgenograms; 14 diagrams and charts; 4 tables.

R. S. ORMOND, M.D.
The Henry Ford Hospital

Aneurysmal Dilatation of the Aortic Sinuses in Coarctation of the Aorta: Report of Two New Cases and Review of the Literature. Israel Steinberg and B. P. Sammons. Ann. Int. Med. **49**: 922–934, October 1958. (I. S., 525 East 68th St., New York 21, N. Y.)

Two cases of coarctation of the aorta with aneurysmal dilatation of the aortic sinuses are reported. One of the patients was a twenty-six-year-old man and the other a thirteen-year-old schoolboy. In each case angiocardiography revealed the aortic sinus aneurysm and the coarcted aorta. In each the coarctation was resected, with end-to-end anastomosis of the aorta and a satisfactory outcome.

The aortic sinuses are intracadiac and cannot be identified on conventional roentgenography. During angiocardiography, they appear as dilatations at the root of the aorta immediately above the aortic valves, being best visualized in the left anterior oblique view. In this view, the right coronary sinus is regularly anterior to and just behind the sternum.

A total of 7 aortic sinus aneurysms associated with coarctation of the aorta and 1 with pseudocoarctation have been diagnosed by angiocardiography. Of these, 6 were from The New York Hospital, 1 was from the U. S. Naval Hospital, St. Albans, N. Y., and the other was found in the literature. The ages of the patients when the diagnosis was first made by angiocardiography varied from thirteen to twenty-seven years, with an average of twenty-one years. Five patients were asymptomatic at the time of admission, although a history of previous hypertension or heart murmurs was present in every instance. Systolic murmurs (Grades 3 to 4) transmitted to the axilla and back, especially over the suprascapular area and similar to those usually found in coarctation, were common.

Elevated upper-extremity blood pressures with diminished-to-absent lower-extremity pressures were present in all but 1 case. The electrocardiogram indicated left ventricular hypertrophy in 4 instances.

The chest roentgenogram revealed significant findings in every case. There was enlargement of the heart, especially the left ventricle, in 6 instances; in 2 cases, the heart was normal in size. Deformity of the aortic arches was a common finding. Rib notching occurred in all but one patient.

The definitive diagnosis of aortic sinus aneurysm is provided by angiocardiography. Aneurysmal dilatation of all of the aortic sinuses was present in 6 cases. Ascending aortic and brachiocephalic arterial dilatations were common, being absent in only 2 instances. Significant dilatation of collateral arteries (mammary, scapular, and intercostal) was observed in every case but the one of pseudocoarctation.

The diagnosis of unperforated aortic sinus aneurysm can be made only by contrast visualization of the aortic root. Angiocardiography, however, is the preferable method of visualizing the aorta because it avoids arterial puncture. Rupture of an aortic sinus aneurysm is often manifested by sudden onset of severe dyspnea, chest pain, right heart overloading and evolution of machinery-like murmurs. Confirmation may be made by cardiac catheterization.

Coarctation of the aorta should be suspected when there are hypertension and diminished (or absent) lower extremity pulses or blood pressure. Confirmation may then be had by roentgen studies of the chest which, in adults, frequently show rib notching, deformity of the arch, and left ventricular enlargement.

All patients except the one with pseudocoarctation, for whom operation was not indicated, had successful resection of the coarctation and end-to-end anastomosis of the aorta.

Although the presence of an unperforated aneurysm of the aortic sinus seems ominous, the prognosis is not necessarily bad. All of the patients in this series are working and engaging in sporting activities; rupture has not occurred. Furthermore, reduction of hypertension by correction of the coarctation of the aorta promises to be beneficial by reducing stress and tendency of the aortic sinus aneurysm to rupture.

Knowledge of the presence of aortic sinus aneurysm associated with coarctation is important, for it will alert the surgeon to the need for hypothermia during surgical resection of the lesion, and will thereby avoid undue stress.

Four roentgenograms; 1 table.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Late Hemodynamic Complications of Anastomotic Surgery for Treatment of the Tetralogy of Fallot. Richard S. Ross, Helen B. Taussig, and Melvin H. Evans. Circulation **18**: 553–561, October (Part I) 1958. (Johns Hopkins Hospital, Baltimore, Md.)

In a study of 17 patients with late complications from artificial shunts, 2 different syndromes were found, both apparently related to shunts which were too large originally or became so by dilatation.

In the one group the picture resembles congestive failure resulting from an arteriovenous fistula. Salient features are tachycardia, systolic hypertension, wide pulse pressure, cardiac enlargement, venous hypertension, hepatomegaly, and fluid retention. In these cases the left ventricle is incapable of handling the load of the systemic flow plus the added volume through the shunt, which is slightly too large.

In the other group of cases the large flow through the shunt somehow causes an increase in pulmonary resistance and consequently an increase in pulmonary artery pressure. As the pulmonary pressure approaches that of the aorta, the flow through the shunt decreases to insignificance. The pulmonary artery becomes very large, polycythemia and cyanosis return, and cardiac failure ensues.

Seven roentgenograms; 1 photomicrograph; 1 photograph; 1 chart; 1 table.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

The Diagnosis of Complete Transposition of Pulmonary Veins. H. Hallerbach and A. Schaede. Fortschr. a. d. Geb. d. Röntgenstrahlen **89**: 152–171, August 1958. (In German) (Medizinische Universitätsklinik, Bonn, Germany)

In transposition of pulmonary veins the lesser circulation is overloaded because oxygenated blood returns from the lungs to the right heart instead of going to the left atrium. This condition leads to hypertrophy and dilatation of the right atrium and ventricle, while the left atrium and ventricle are relatively small or even underdeveloped. The subsequent course is myocardial insufficiency and sclerosis of the pulmonary arteries.

Complete transposition of pulmonary veins is not compatible with life unless there is an associated right-to-left shunt through an atrial septal defect or a patent foramen ovale. Partial transposition occurs more frequently than the complete type. The right pulmonary veins are affected twice as frequently as the left. Symptoms are present only when there is involvement of more than 50 per cent of the pulmonary veins.

The anomalous veins may lead to the coronary sinus, the vena cava or branches, the vena subclavia and azygos, a persistent left superior vena cava, and even to the vena portae and the ductus venosus. In total transposition, only mixed blood can reach the peripheral arteries *via* a right-to-left shunt. Therefore, the oxygen content of these arteries is equal to that of the right atrium, a matter of decisive diagnostic importance. A correct diagnosis is essential for proper planning of complicated surgical repairs.

In a group of 2,000 cardiac investigations, complete transposition of pulmonary veins was found in 20 (1 per cent). In these cases there was right heart enlargement with and without hilar dance. Occasionally, an abnormal vascular pattern was noted, especially on tomograms, but this was not entirely conclusive diagnostically. Cardiac catheterization of the right atrium and ventricle was very informative, but the tip of the catheter could rarely be guided into the left atrium. The intracardiac pressure was moderately increased in the right heart, especially in the right ventricle. Oxygen content of the right heart was higher than in the venae cavae, but a diagnosis of complete transposition was valid only when the oxygen values in the right atrium were the same as in the peripheral arteries.

Angiocardiographic findings were similar to those of atrial septal defect, as a constant dilution through a jet stream from the anomalous pulmonary veins prevented a satisfactory contrast of the right heart. There were 8 cases in which all veins led to the right atrium, and in 3 the veins terminated at the coronary sinus. In 4 additional cases the veins led partly to the superior vena cava and the right atrium, respectively. In the remaining 5 cases the veins drained into a persistent left superior vena cava and tributaries. Only in these cases was the superior mediastinum distinctly widened, resulting in the characteristic "figure 8" configuration. There was significant increase of oxygen content in the superior vena cava with typical dilution of the contrast medium. Catheterization also revealed marked saccular dilatation of the affected veins.

This article is well illustrated by 75 roentgenograms and by schematic drawings.

ERNEST KRAFT, M.D.
Northport, N. Y.

Angiocardiographic Observations in Mitral Disease with Special Reference to Volume Variations in the Left Atrium. Håkan Arvidsson. Acta radiol. Suppl. 158, 1958. (Södersjukhuset, Stockholm, Sweden)

The material for this study comprised 73 angiocardiographic examinations on 69 patients. Both preoperative and postoperative studies were made in 4 cases of mitral stenosis in order to ascertain the effects of commissurotomy. All patients were subjected to thorough clinical cardiologic examination, including conventional heart roentgenography. In this way, the total volume of the heart as well as the heart volume per square meter of body surface were determined.

Angiocardiography was performed with a film changer of the roll-film type capable of six exposures per second in two planes at right angles (see Gidlund: Acta radiol. Suppl. 130, 1956. Abst. in Radiology 69: 462, 1957). Contrast solution was injected into the main stem of the pulmonary artery with the aid of a heart catheter after venous catheterization. Several different contrast solutions were tried, and Urografin was found to be the least toxic. The size of the dose and rate of injection varied. In the majority of cases, general anesthesia with endotracheal intubation was used. Complications occurred in 2 patients, namely, pulmonary edema, developing immediately after injection but with no permanent after-effects.

In order to obtain a maximum number of films showing opacification of the left side of the heart, a programme selector was utilized. Following views of the pulmonary artery, a pause was made during the "pulmonary capillary phase" to allow passage of contrast medium through the lungs. This interval varied from one to six seconds, depending on the size of the heart, and the pressure in the pulmonary circulation. After the pause six exposures per second were made for as long as the left side of the heart and the aorta were opacified.

By measuring the atrial volume in all films in which the atrium was opacified, its variations during the cardiac cycle could be studied. This was accomplished by considering the atrium to be ellipsoid in shape as seen on anteroposterior and lateral projections. The reason why the dilated atrium is projected in this shape rather than as a sphere is explained by impediment to enlargement in certain directions by adjoining organs. Also studied were left ventricular volume and thickness of the left ventricular wall in diastole.

Various methods have been tried for the angiocardiographic differential diagnosis of mitral disease, including anatomic changes of the heart chambers and the speed with which contrast solution passes through the heart. Dilatation of the left atrium is often the earliest sign of mitral disease, but this is not the only condition in which enlargement occurs, the left atrium dilating to a greater or lesser degree in connection with all disturbances of left ventricular function. Different opinions have been expressed regarding the significance of left atrial size in the differential diagnosis between mitral stenosis and insufficiency. In this series, a very large atrium was not present unless there was an insufficiency component in the mitral orifice.

Magnitude of volume variation in the left atrium as a diagnostic aid has been previously studied, primarily by means other than angiocardiography. In this investigation the left atrial volume variation constituted the main subject of study, and it was found that in the majority of cases the maximum volume changes were greater in mitral insufficiency than in stenosis. Of even greater value for the differential diagnosis was the course of the volume variation during the heart cycle. A disadvantage of the volume analysis is that it is relatively difficult technically, and is time-consuming.

Maximum diastolic volume of the left ventricle proved of importance, for if the maximum left ventricular volume was normal or less than normal it was very probable that pure stenosis was present. Also, there was only a very small amount of residual blood in the left ventricle in pure uncomplicated mitral stenosis.

The appearance of the mitral orifice was of great significance. Study of the mitral valve on lateral view revealed a characteristic distention of the leaflets which took place during diastole in the majority of cases of stenosis. In mitral insufficiency this ballooning did not occur. The leaflets were often thickened and the posterior cusp is frequently shortened. No characteristic movement pattern was observed.

Results were divided into a considerable number of groups based on cardiac pathology and included mitral stenosis with sinus rhythm, and with fibrillation; predominant mitral insufficiency with sinus rhythm, and with fibrillation; and various combinations of mitral stenosis, mitral insufficiency, and aortic stenosis with sinus rhythm, and with fibrillation.

The author concludes by stating that conclusive angiocardiographic diagnosis must be based on a study of the left atrium, mitral cusps, left ventricle, and aortic orifice. The mitral orifice, the seat of the pathological process causing disturbance in the hemodynamics, constitutes the most important subject for study, but even if the ostium cannot be directly observed, the diagnosis can be obtained from indirect signs such as volume differences in the left atrium, atrial volume curve, and size of the left ventricle. One should not, however, be misled into believing that angiocardiography may be used as an independent diagnostic method, for results should always be correlated with the clinical findings.

This detailed monograph contains a considerable amount of specialized data, and includes 23 case reports with 26 graphs, 3 tables, 4 diagrams and 29 roentgenograms. CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

The Correlation Between Various Assessments of Pulmonary Arterial Pressure in Mitral Stenosis. J. F. Boyd, S. D. Scott Park, and George Smith. Brit. Heart J. **20:** 466–470, October 1958. (University of Glasgow, Scotland)

In 50 patients who had undergone commissurotomy for mitral stenosis, radiological studies were compared with other means of estimating the pulmonary vascular status.

Roentgen study was usually on the basis of plain films, with special attention to the size of the heart, pulmonary artery, hilar and peripheral branches, horizontal lines, hemosiderosis, old infarcts, and pleural thickness.

Lingular biopsies provided histological material in which the ratio of wall thickness to vessel lumen was measured in the small arteries.

Artery pressures were measured by catheter and directly at the time of surgery.

Radiological, clinical, and histological assessments correlated well, so that the authors conclude that an accurate estimate of the pulmonary vascular status can be made from study of plain films, measurement of pulmonary artery pressure, and the degree of disability.

Two roentgenograms; 2 photomicrographs; 1 graph; 7 tables. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Radiological Observations on 33 Cases of Primary Interstitial Myocarditis During an Outbreak in the Haifa Area. J. Munk and K. T. Lederer. J. Fac. Radiologists **9:** 195–203, October 1958. (Rambam Government Hospital, Haifa, Israel)

The authors examined radiologically 33 children

with primary interstitial myocarditis out of a total of 61 seen during an outbreak in the Haifa area (Israel) between May 1956 and December 1957. Fifty of the children died, and in all these, except one, the diagnosis was confirmed postmortem. The age of the patients ranged from six months to three and a half years.

The radiologic features of the disease are described:

(1) *Size and shape of the heart.* General enlargement of the heart is the predominant feature of the disease and was invariably seen. In cases that permitted further observation, gradual decrease of heart size, with eventual return to normal, was demonstrated.

(2) *Passive pulmonary congestion* was present in all but 4 cases. In the majority of cases the appearance was typical, with arterial, venous, and lymphatic engorgement extending into the most peripheral parts of the lung fields together with Kerley's B lines. Some patients showed marked emphysema, which is explained by expiratory impairment. In addition, the haziness of the lung fields was less marked than in the more typical group, and the pathological interstitial pattern was shown mainly in the paramediastinal regions, leaving the peripheral zone free.

(3) In all but 5 cases *pleural fluid* was seen as a band-like shadow along the lateral chest wall, sometimes unilateral, sometimes bilateral.

(4) *Pulsations of the heart.* Sixteen of the patients were fluoroscoped and these showed very weakened or indistinguishable cardiac pulsations. Judging the amplitude of the pulsations was difficult because of tachycardia, which was present in most of the cases. An important sign of the beginning of recovery (under digitalis treatment) is the reappearance of visible pulsation.

The radiological differential diagnostic considerations are discussed. The most important task of the radiologist is the differentiation between acute inflammatory pulmonary disease and myocarditis; the presenting severe clinical signs in both these conditions may make a clinical differentiation difficult.

Nineteen roentgenograms; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

Examination of the Thoracic Aorta and Left Ventricle by Intraventricular Catheterization via the Femoral Artery. G. Bonte, J. Caron, M. Pauchant, and A. Gérard. J. de radiol. **39**: 593–598, October 1958. (In French) (Cité hospitalière, Lille, France)

After discussing various means of opacifying the left ventricle the authors describe their method based on the Seldinger technic (Acta radiol. **39**: 368, 1953. Abst. in Radiology **62**: 466, 1954). A polyethylene catheter is introduced into the femoral artery and followed by means of fluoroscopy up to the level of the ascending aorta and then down into the left ventricle. The 14 patients who were examined by this procedure tolerated the study well. The electrocardiograms showed a few extrasystoles and occasionally transitory bradycardia.

It is quite possible that the method may be applied to the diagnosis of mitral insufficiency, aortic insufficiency, and, occasionally, congenital heart disease with septal defects. It may also be useful in the study of the coronary arteries.

Twelve roentgenograms.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Percutaneous Selective Angiography of the Coeliac Artery. Per Ödman. Acta radiol. Suppl. 159, 1958. (Karolinska Sjukhuset, Stockholm, Sweden)

The term "percutaneous selective coeliac angiography" describes the author's technic in which a radiopaque polyethylene catheter with a preformed curve at the tip is inserted through one of the femoral arteries and guided up the aorta under fluoroscopic control; the tip is maneuvered into the mouth of the coeliac artery and contrast medium is injected through the catheter while serial films are rapidly exposed by means of biplane radiography. A preliminary account of the method has been published (Acta radiol. **45**: 1, 1956. Abst. in Radiology **67**: 773, 1956).

This monograph presents an amplification of the earlier report but, unlike it, is concerned strictly with visualization of the coeliac artery, its many branches, the upper abdominal viscera, and the venous return. The technic has been applied in 61 angiographic examinations on 58 patients. Fourteen controls afforded normal angiographic measurements for comparison. Pathologic conditions were disclosed in 45 examinations on 43 patients. These were classified in 7 groups according to the angiographic findings, under the following headings: I. Cirrhosis of the liver. II. Splenomegaly not due to cirrhosis. III. Cancer of the stomach. IV. Intrahepatic neoplasms. V. Disorders of the pancreas. VI. Retro- and intraperitoneal expansive processes. VII. Miscellaneous conditions.

The desirability of a radiologic method of diagnosis of morbid processes of the pancreas, liver, and spleen has long been recognized. The pancreas, particularly, has been difficult to delineate. Selective arteriography of the coeliac artery provides a safe means of obtaining detailed information concerning these organs while avoiding some of the inadequacies of phlebographic and general aortographic procedures as well as the risks attendant upon injections of larger quantities of opaque media.

The work presented here is thoroughly documented and quite detailed. The complete description of equipment and medication, anatomical observations, methods of mensuration, and the numerous tabulations do not lend themselves to abstracting.

The text is divided into three parts and provides a particularized analysis of (1) the technic, (2) the results (including normal anatomical appearance and measurements and pathologic angiographic findings), and (3) conclusions concerning the tolerance to contrast media based on animal experiments.

The paper contains much practical information. The radiographic reproductions are good, although they are positive prints. The equipment that is required for the procedure is certainly not available in the average smaller institution or private office, but those who are doing this kind of work should find the monograph of value and interest.

Eighty-one roentgenograms; 56 charts and diagrams; 14 tables.

JOHN F. RIESSER, M.D.
Springfield, Ohio

Unilateral Renal Injury Due to Translumbar Aortography. C. G. Clark. Lancet **1**: 769–770, April 12, 1958. (Aberdeen Royal Infirmary, Aberdeen, Scotland)

A case of severe unilateral renal injury following translumbar aortography is reported This case is of

special interest because of the absence of symptoms. If the implications of direct injection of organic iodide into the renal artery had not been appreciated, the lesion probably would have gone unrecognized.

The patient was a 64-year-old man, in whom a diagnosis of thrombosis of either the right common iliac artery or the right external iliac artery was made. Fifty milliliters of 70 per cent sodium acetrizoate (Diaginol) was injected directly into the right renal artery, and the aorta was filled by overflow. Occlusion of the right common iliac artery and part of the external iliac artery was demonstrated. After aortography, no abnormal constituents were found in the patient's urine, and the specific gravity varied from 1.018 to 1.024. There were no symptoms or signs of injury to the right kidney. Output of urine was never less than 800 ml. in twenty-four hours, and the blood urea level was 40 mg. per 100 ml. Although there was no positive evidence of renal damage, it seemed advisable to postpone intravenous urography rather than subject the kidneys to further exposure to organic iodide. When pyelography was performed about a month later, it showed a normal left kidney but poor concentration in the right. The urine contained no albumin, cells, or casts, and the specific gravity was 1.022. The next day an aortofemoral shunt homograft was inserted to bypass the thrombosed iliac segment. Four months following aortography the ureters were catheterized and indigo-carmine was injected intravenously. There was good concentration of the dye on the left side, but on the right there was no obvious excretion at the end of an hour. The patient was in good health and the graft was functioning.

The factors responsible for renal damage following aortography are discussed, and the conclusion is drawn that a safer contrast medium is required.

Two roentgenograms.

Internal Diameter of Renal Artery and Renal Function. N. S. R. Maluf. Surg., Gynec. & Obst. **107:** 415–428, October 1958. (Kaiser Foundation Hospital, Los Angeles, Calif.)

By means of translumbar aortography the author shows an association between the caliber of the main renal artery or arteries and the magnitude of renal function. The method of translumbar aortography and the measurement of the renal arteries from the roentgenograms are discussed. In 18 young patients with two essentially normal kidneys the internal diameter of the renal artery was found to be 6.5 to 6.7 millimeters with a standard deviation of 0.75 to 0.88, whereas, in 9 young patients with only one healthy hypertrophied kidney, the internal renal artery diameter was 8.4 to 8.6 millimeters, with a standard deviation of 0.71 to 0.83.

To cancel out differences in caliber due to size, sex, and age of patient, the author uses the ratio of renal artery diameter to splenic artery diameter. Since the normal renal artery is characteristically wider than the splenic artery, the ratio normally is greater than one. The ratio rises in renal hypertrophy and adenocarcinoma of the kidney; it falls in renal hypoplasia, congenital polycystic kidneys, and chronic hydronephrosis; it remains unchanged in kidneys with large solitary cysts or acute hydronephrosis.

A narrow renal artery is always indicative of reduced renal function. The intensity of the instantaneous nephrogram is also a reflection of kidney function. Both the renal artery size and the nephrogram intensity should be considered before a kidney is termed completely atrophic.

The author feels that translumbar aortography gives valuable information about potential renal function, particularly in cases of prolonged unilateral ureteral obstruction when retrograde catheterization is impossible and the kidney is not visualized by intravenous injection of an organic iodide.

Twelve roentgenograms; 6 photomicrographs; 4 photographs; 1 diagram; 4 tables.

ROBERT E. CAMPBELL, M.D.
University of Pennsylvania

Anomalous Artery in Intralobar Bronchopulmonary Sequestration. Report of Two Cases Demonstrated by Angiography. Franklyn P. Gerard and Harold A. Lyons. New England J. Med. **259:** 662–666, Oct. 2, 1958. (State University of New York, Brooklyn, N. Y.)

The authors present two cases of intralobar bronchopulmonary sequestration in which the anomalous artery was demonstrated by angiographic studies. It is this anomalous artery, arising from the aorta either above or below the diaphragm and supplying the area of sequestration, that, when the condition has not been recognized, has led to serious operative mishaps and death. Angiographic examination, therefore, should become a part of the diagnostic procedure in every suspected case of bronchopulmonary sequestration.

In both of the cases reported here the anomalous arteries were clearly demonstrated before surgery. Their recognition depends upon opacification of the aorta. The authors advocate the venous angiocardiographic method of Robb and Steinberg for its ease of performance, adequate visualization of the entire aorta, and its safety. Because the Sanchez-Perez seriograph is too slow for a good study in children, aortography was considered necessary in one of the cases. This is a valuable procedure and may at times be considered necessary when angiocardiography has failed.

The hazard of surgery without the foreknowledge of the presence of the anomalous vessels is emphasized.

Seven roentgenograms; 2 diagrams.

THEODORE E. KEATS, M.D.
University of Missouri

Selective Cine-Angiocardiography with Image Intensification. Hamish Watson, C. Pickard, K. G. Lowe, and Ian Hill. Brit. Heart J. **20:** 459–465, October 1958. (University of St. Andrews, Dundee, Scotland)

This is essentially a general discussion of the advantages of selective injection of contrast medium into carefully chosen sites, followed by cineangiocardiography with image intensification. The field is small, but this is not too serious a difficulty in children, in whom investigation of congenital cardiac lesions is usually done. By this method the most information for the least radiation is obtained and the films can be studied by still or moving projection. Faint filling is seen more readily on the motion pictures. Synchronization of exposures with the cardiac cycle is naturally important.

The method can be improved by the development of

faster film so that true slow motion projection may be obtained.

Twenty-four roentgenograms; 1 photograph; 1 diagram. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

THE DIGESTIVE SYSTEM

Esophageal Webs: A Report of 58 Cases and an Attempt at Classification. Munir H. Shamma'a and Edward B. Benedict. New England J. Med. **259:** 378–384, Aug. 21, 1958. (E. B. B., Harvard Medical School, Boston, Mass.)

A series of 58 cases of esophageal webs, all with difficulty in swallowing, is reported. Fifty-one of the patients were females; 95 per cent were over thirty years of age. The webs were demonstrated by esophagoscopy, radiologic study, or open operation. X-ray studies were performed on 56 patients and were positive in all but 4 cases. Esophagoscopy was done in 50 cases and the web was not seen in 6.

The cases are classified as follows: (1) upper esophageal webs, with anemia, without anemia, and with no hematologic data; (2) middle esophageal webs; (3) lower esophageal webs; (4) webs associated with benign mucous-membrane pemphigus.

Upper esophageal webs with anemia (Plummer-Vinson syndrome) were found in 23 patients, all women. All had hypochromic anemia; 14 had smooth red tongues. Spooning of the nails was a less common finding. Radiologic examination was performed in all 23 cases, definitely demonstrating the web below the cricoid cartilage in 20 cases and equivocally in 1. The web was a thin diaphragm partially crossing the esophagus, seen best in the lateral view. Treatment consisted of esophagoscopy with divulsion of the web, bougienage, and/or iron therapy.

Upper esophageal webs without anemia were present in 14 patients (12 females and 2 males). In 11 patients with upper esophageal webs no hematologic data were available.

Webs of the middle third of the esophagus were seen in 2 patients. One, a seventy-year-old woman, was treated by divulsion. Histologic study showed hyperkeratosis of the epithelium. The other patient was a man of thirty-nine with apparently caustic strictures treated by bougienage.

Four patients had lower esophageal webs, and none of these showed anemia. One was an eleven-month-old boy with a fibrous stricture in the wall of the esophagus. In 2 patients, 1 male and 1 female (both in the sixth decade), esophageal rings were associated with a sliding hiatus hernia; this was repaired with relief. The fourth case apparently developed secondary to an ulcer.

In 4 instances webs were associated with benign mucous-membrane pemphigus. In 1 of the patients cancer of the lips and cheek developed.

The association of esophageal webs and carcinoma is again noted. In 9 of the patients (16 per cent) in this series carcinoma of the buccal mucosa or esophagus developed. In 3 of the 6 with carcinoma of the esophagus, two or more webs were present. Seven patients had disease of the thyroid gland. The frequent finding of hypothyroidism in Plummer-Vinson syndrome suggests further study.

Pathological study of the webs was not remarkable, revealing a normal squamous epithelial layer with an underlying connective tissue layer and perhaps a mild chronic inflammation with mononuclear cells.

Two roentgenograms; 1 photograph; 4 tables.
GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

Esophagobronchial Fistula. E. Schwarz and M. Berger. Schweiz. med. Wchnschr. **88:** 688–690, July 12, 1958. (In German) (Chirurgische Klinik der Universität Zürich, Switzerland)

The authors report a case of esophagobronchial fistula in a thirty-year-old patient. While this was believed to be congenital, it did not produce symptoms until after two bouts of right lower lobe pneumonia, followed by prolonged cough; attacks of coughing also occurred following ingestion of cold liquids. The fistula was demonstrated preoperatively with a very thin mixture of barium while the patient was lying on his right side. Resection of the lesion was successfully carried out.

Two roentgenograms; 1 photomicrograph; 1 photograph. JULIUS HEYDEMANN, M.D.
Chicago, Ill.

Some Radiological Observations on the Effect of Morphine Sulphate on the Gastro-Intestinal Tract in Man. F. S. Grebbell. Brit. J. Radiol. **31:** 534–541, October 1958. (Royal Victoria Hospital, Belfast, Northern Ireland)

The authors investigated the action of morphine on the gastrointestinal tract, using 20 volunteer subjects, none of whom had any gastrointestinal symptoms prior to or at the time of the examination. Ten of the group served as controls.

The following changes were observed radiologically after intravenous injection of morphine sulfate:

(1) There was an increase in tone and in the amplitude of the peristaltic waves of the stomach.

(2) The effect on the gastric peristaltic waves lasted approximately thirty minutes, after which it gradually diminished, the amplitude of the waves becoming much less.

(3) There was no evidence to suggest an increase in the frequency of the peristaltic waves.

(4) There was a delay in gastric emptying (9 of 10 subjects).

(5) There was no evidence of pylorospasm.

(6) Gastric emptying continued during the period of increased tone.

(7) There was no evidence of a tonic contraction of the duodenum.

(8) Dilatation of the duodenum occurred in 8 of 10 subjects.

(9) There was an increase in the "restless activity" of the small intestine.

(10) Dilatation of the ileum occurred in 8 of 10 subjects.

(11) The transit time to the cecum was increased.

(12) There was an increase in cecal tone and activity.

(13) There was no evidence to suggest contraction of the ileo-cecal sphincter.

None of the subjects examined showed any marked ill effects following the injection of morphine. The intravenous injection apparently minimizes the side reactions.

Ten roentgenograms; 5 tables.
THEODORE E. KEATS, M.D.
University of Missouri

Torsion of the Stomach as a Cause of Vomiting in Infancy. S. Eek and H. Hagelsteen. Lancet **1:** 26-28, Jan. 4, 1958. (Children's Department, University Hospital, Oslo, Norway)

Many infants recorded as having neuropathic or habitual vomiting are actually suffering from torsion of the stomach. In the past six or seven years, the authors have observed this condition in 54 children, ranging in age from one day to three years.

Normally the stomach is fixed at two points—the cardia and the pylorus. At the cardia it is fixed by the upper part of the hepatogastric ligament and by the gastrosplenic ligament. At the pylorus the duodenum is fixed behind the peritoneum. The rest of the stomach is suspended freely by the hepatogastric ligament. The transverse colon is normally suspended below the greater curvature of the stomach by the thin and short gastrocolic ligament. In infants the lower thoracic aperture is relatively open and the liver easily mobile. In the supine position the anterior edge of the liver descends, and a space may open between the liver and the anterior abdominal wall, into which a gas-filled transverse colon may easily rise. In these circumstances the transverse colon pulls the stomach and twists it on its longitudinal axis with the cardia and pylorus as fixed points. In the authors' experience this twisting has never been more than 180° and it can be less. The twisting may delay gastric emptying, interfere with peristalsis, and perhaps also disturb the circulation of the blood in the stomach. The chief symptom is vomiting, sometimes projectile and usually beginning soon after birth.

Torsion is best demonstrated when the roentgen examination is carried out with the patient in the erect position. Findings were strikingly alike in all the authors' cases. The body of the stomach is raised, with the greater curvature as the highest point and the lesser curvature as the lowest. The posterior wall of the stomach points forward, and the pyloric antrum and pylorus with the duodenal bulb are directed more or less straight down. The middle part of the transverse colon is interposed between the liver and the anterior abdominal wall and comes above and in front of the stomach, often even just under the diaphragm.

Treatment of torsion of the stomach in the infant is very simple. The patient should be placed prone, with the upper part of the body lowered, or alternatively merely placed on his right side. Usually vomiting will cease immediately or become noticeably less. In a few cases it may continue for some time. In no case in the authors' series was it necessary to untwist the stomach surgically. Attempts to reduce the torsion by filling the stomach with barium, in the hope that the weight of the barium might bring the transverse colon back into normal position, have been unsuccessful.

Fourteen roentgenograms; 2 photographs; 2 drawings; 2 graphs.

Giant Hypertrophic (Tumour Simulating) Gastritis. P. E. S. Palmer. J. Fac. Radiologists **9:** 175-182, October 1958. (Bulawayo, Southern Rhodesia)

The author reports 5 cases of giant hypertrophic gastritis. This is a very definite condition which is based on pathological findings as well as on radiological and gastroscopic investigations. The normal mucosal pattern is replaced by grossly hypertrophied and distorted rugae, associated with thickening of the stomach wall and a generalized increase in the size of the stomach. The condition is usually chronic but can be completely reversible. An accurate clinical diagnosis cannot be made.

Radiologically the changes in the stomach fall into three well defined groups. In the group in which most cases occur, the middle third of the stomach is affected in two ways, which can be seen in the same patient either at the same time or in successive examinations. There are massive irregular rugae on the posterior wall and greater curvature of the stomach. In some cases the height and width of the folds are such that the mucosal pattern may be difficult to see and the stomach wall shows an irregular coarse thickening, with decreased peristalsis, and is less pliable than usual. In the other variety the mucosa is so hypertrophied that the stomach appears filled with marbles—the condition of diffuse or multiple polyposis. The stomach wall is also stiff and peristalsis is decreased.

In the second group—the type usually described as "tumor simulating gastritis"—the most striking finding is large tumor-like masses in the fundus of the stomach. The mucosa is smooth and if the pattern is visible it is distorted, as if normal gastric mucosa were stretched over an underlying tumor. In this group there is frequently associated gastric ulceration, demonstrable radiologically, whereas in the previous group any ulceration is obscured by the mucosal hypertrophy.

Cases of the third group are least common and, because the pyloric region is affected, the most dramatic and difficult to diagnose. Symptoms include recurrent vomiting and frequently pain. Radiologically there are gross hypertrophied folds of mucosa with thickening of the stomach wall involving the distal third of the stomach. Prolapse of the mucosa can occur, and bleeding is not infrequent.

The differential diagnosis of giant hypertrophic gastritis from malignant disease is a problem in which gastroscopy, hematology, or biochemistry cannot help. The condition is benign and is not cured by surgery, which is indicated only when there is severe hemorrhage. The etiology is unknown and there is no specific treatment. A strict ulcer regimen will afford relief.

Ten roentgenograms; 2 photomicrographs; 1 photograph.

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Technical Surgical Factors Which Enhance or Minimize Postgastrectomy Abnormalities. William E. Abbott, Harvey Krieger, and Stanley Levey. Ann. Surg. **148:** 567-591, October 1958. (Western Reserve University School of Medicine, Cleveland, Ohio)

This is a lengthy, primarily surgical paper which concerns the abnormalities of upper gastrointestinal physiology and function following various operative procedures. Particular attention is directed toward the "dumping syndrome," in respect to its mechanism of production and its avoidance. Approximately 100 subjects, including several normal persons, were studied by serial filming of the abdomen following ingestion of a barium-food mixture. Films were made at approximately ten-minute intervals for the first sixty to ninety minutes and at somewhat longer intervals thereafter. The patients were maintained in an upright position so that the study might simulate as closely as possible the usual conditions following ingestion of food.

Results are presented for numerous patients following a wide variety of gastric and gastrointestinal operations.

It appears that the primary etiologic factor producing the "dumping syndrome" (anorexia, weight loss, poor nutrition, diarrhea, vasomotor disturbances) is rapid flooding of stomach contents into the upper small intestine. The amount of dumping or flooding can be closely correlated with the size of the anastomotic stoma and the rate of gastric emptying as shown by the barium-food x-ray studies. Best results were consistently shown in patients who had small stomas and a gastric emptying time approximating normal. The diagnosis of the "dumping syndrome" can be made only by determining the rate of gastric emptying.

It is possible that some "dumping" symptoms may follow distention and stasis in the stomach or afferent loop. Again barium-food x-ray studies furnish a reliable objective method of differentiating this set of circumstances from the usual "dumping syndrome."

The authors feel that in their own group of patients the best results have been obtained with hemigastrectomy, vagotomy, and small stoma gastroduodenostomy. An internal diameter of the stoma less than 2 cm. is desirable. Presence of mucosal folds or deformities at the stoma from surgery may alter the effective stomal size. These features can usually be appreciated by proper radiographic studies.

Ninety-six roentgenograms; 12 diagrams.

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Roentgenologic Diagnosis of Duodenal Ulcers. Abércio Arantes Pereira. Bol. da Soc. brasil. de radiol. **2**: 1–40, January–February 1958. (In Portuguese) (Hospital Moncorvo Filho, Rio de Janeiro, Brazil)

This is an excellent, almost didactic monograph, based on 2,600 examinations with the barium meal, performed on 2,379 patients between January 1952 and December 1956. Duodenal ulcers were present in 417 (21.5 per cent) of 1,966 patients seen in a private hospital and in 64 (15.5 per cent) of 413 from a teaching institution. In the total of 481 patients with duodenal ulcer, the condition was associated with cascade stomach in 36 (7.5 per cent), with gastric ulcer in 17 (3.5 per cent), with hiatus hernia in 7, with prolapse of the gastric mucosa in 3, and with gastrojejunostomy in 2.

In the 1,966 private patients, ulcer appeared to be six times more frequent than other pathologic findings in the duodenum. There were 74 lesions (3.7 per cent) not associated with ulcer. These included duodenal diverticula in 33, mucosal prolapse in 17, mesenteric artery syndrome in 13, extrinsic pressure from the pancreas in 4, bulbar polyp in 2, carcinoma of the duodenum in 2, and 1 case each of tumor of the angle of Treitz, of adhesions, and of stenosis of the second portion of the duodenum.

Among the 417 private patients with duodenal ulcer, there was a well filled, smooth bulb with niche in 35 (8.4 per cent), a deformed bulb with crater in 195 (46.7 per cent), and a deformed bulb without demonstrable niche in 187 (44.8 per cent). That is, the crater could be proved in only 230 (55.1 per cent) of the cases. This emphasizes the need for accurate evaluation of secondary signs of duodenal ulcer, namely (1) elongation of the pyloric canal, (2) persistently filled bulb, (3) spot tenderness on pressure, (4) reduced mobility of the bulb, (5) exaggerated bulbar motility, (6) gastric changes (hypertonicity, hyperperistalsis, hypersecretion, pylorospasm, etc.), and (7) pronounced mucosal pattern in the bulb.

Ninety-five roentgenograms; 5 sketches; 6 tables.

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Postbulbar Duodenal Ulceration. Lorna Cooke and Charles F. Hutton. Lancet **1**: 754–757, April 12, 1958. (Central Middlesex Hospital, London, N. W. 10, England)

The diagnosis of postbulbar duodenal ulcer is often missed and, as a result, patients with a severe and even lethal lesion may be regarded as neurotic. Even laparotomy may fail to disclose the ulcer. Nevertheless, diagnosis is nearly always possible roentgenologically if appropriate technics are employed, especially if there is close co-operation between radiologist and clinician. The present article is mainly concerned with ulcers in the immediate postbulbar area.

Two groups of patients can be singled out in whom a tentative clinical diagnosis can be made: the *hemorrhage group*, with a long history of pain and one or more attacks of bleeding, and the *intermittent obstructive group*, with a history of repeated attacks of profuse vomiting and severe pain, lasting a few days. The most important symptom is hemorrhage, for it is often severe and hard to control by medical means.

Postbulbar ulceration cannot be excluded until the immediate postbulbar area has been fully visualized. By using a small quantity of barium cream, and taking serial films of the region in more or less exaggerated prone and supine positions, one can examine it without it being obscured by the bulb or pyloric antrum. An overfilled stomach, may, however, make examination impossible. The authors have found it of value in extremely difficult cases, especially in hypersthenic patients, to give a small quantity of barium cream, manipulate this into the bulb and second part of the duodenum, and then inflate the stomach through the stomach-tube. After suitable rotation of the patient, the postbulbar area can be visualized through the air-inflated pyloric antrum. If satisfactory results cannot be obtained in this way with the patient erect, the same technic can be used in the supine or prone position.

The two cardinal radiological features are the demonstration of the crater itself and of any localized stenosis of the duodenum near the ulcer. In addition, it may be possible to observe local alteration of the mucosal-relief pattern around the ulcer. The appearance of the crater is similar to that found in the bulb. The local stenosis, which is usually present, must be distinguished from incomplete filling of the duodenum or constriction due to normal peristaltic waves.

In the differential diagnosis the following conditions must be considered: diverticulum, adhesion band, carcinoma of pancreas, annular pancreas, benign and malignant tumors.

At the Central Middlesex Hospital (London), in the years 1949–1955, 25 cases of postbulbar duodenal ulceration were diagnosed. Twenty-three of the patients were men and 2 women. The average number of barium-meal examinations carried out in this series before a diagnosis was made was 3 (range 1 to 8).

Fifteen patients at some time had hematemesis or melena, generally the latter, and bleeding was severe and difficult to control. Five patients had a history suggesting intermittent upper intestinal obstruction. One case in each group is presented. A third case is reported in which duodenal obstruction became persistent.

Medical treatment is usually unsatisfactory in postbulbar ulceration. Surgery is indicated in most cases and should be undertaken when the patient is relatively well.

Four roentgenograms; 1 drawing; 1 table.

X-Ray Manifestations of Peptic Ulceration During Corticosteroid Therapy of Rheumatoid Arthritis. Theodore F. Hilbish and Roger L. Black. Arch. Int. Med. **101:** 932–942, May 1958. (National Institutes of Health, Bethesda 14, Md.)

In a series of 49 patients treated with corticosteroids for rheumatoid arthritis, 12 peptic ulcers developed. This is an appreciably higher incidence of ulceration than in patients undergoing other types of therapy for rheumatoid arthritis. The atypical signs and symptoms of ulceration occurring in these patients merit reemphasis.

In the authors' experience valuable indirect manifestations of ulceration, such as reflex motor disturbances, tenderness, and edema, may be completely lacking in patients with active ulcers while receiving corticosteroid therapy. Every skill and technic must be used to demonstrate an ulcer crater. Fluoroscopic findings may be entirely normal, but compression films, air-contrast studies, and large films in various projections may disclose the presence of a small crater. A deformed duodenum may be demonstrated in some cases and, if found in a patient shown to have a normal duodenum prior to onset of therapy, may be regarded as presumptive evidence of an ulcer.

Histologically, peptic ulcers developing in corticosteroid-treated patients are interesting in that they commonly show very little evidence of surrounding edema and inflammation. The ulcer margins are sharp and punched out. Fibrosis is minimal, and few adhesions or other signs of attempt at tissue repair are encountered. The pathological findings are consistent with the rapid clinical course of some of these patients, who may suddenly bleed profusely from the gastrointestinal tract after only minimal warning symptoms of peptic ulceration.

Patients receiving corticosteroids deserve careful questioning concerning epigastric distress, and routine stool examinations for occult blood are advisable. A thorough and careful search for ulcer crater formation should be made in any patient experiencing even vague epigastric pain.

Six typical cases are reported, including 2 in which fatal hemorrhage occurred.

Fifteen roentgenograms; 1 photomicrograph; 1 table.

The Incidence of Peptic Ulcer Among Patients on Long Term Prednisone Therapy. Lawrence E. Meltzer, Albert A. Bockman, William Kanenson, and Abraham Cohen. Gastroenterology **35:** 351–356, October 1958. (Philadelphia General Hospital, Philadelphia, Penna.)

The impression that corticosteroids are potentially ulcerogenic has gradually received widespread acceptance in clinical medicine, in spite of conflicting evidence presented and the small number of significant clinical studies. The authors approached this problem by a study of 115 patients who were treated by prednisone for various diseases. These patients were divided into two groups. Group I consisted of 55 patients who had been receiving prednisone for an average of 11.2 months and served for determination of ulcer incidence. Group II was made up of 60 patients examined before initiation of prednisone therapy and again after its continuance for 5.2 months.

Six of the patients in Group I (10.9 per cent) had evidence of duodenal ulcer. Two of these showed active ulceration and in 4 there were chronic radiographic changes. In 2 of the 6 there was a history of peptic ulcer, proved by x-ray, before therapy, while another 2 patients gave an earlier history typical of ulcer but without radiographic study. No gastric ulcers were found in this group.

In Group II the preliminary films showed deformities of the duodenum in 6 (10 per cent), but no active ulcers. No gastric lesions were detected. Following prednisone therapy no active ulcers were noted in any patient and the 6 patients with deformity showed no activation. The maintenance dose of prednisone was 14.2 mg. daily.

Combining both groups, the incidence of active ulcer was 1.7 per cent, which is lower than the incidence in the general population. The incidence of reactivation of old ulcer was 8.3 per cent under prednisone therapy, which is far below the natural history of the disease. On the basis of this study the authors conclude that prednisone is not ulcerogenic.

Two tables.

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The Radiological Investigation of the Small Intestine in Tropical Idiopathic Malabsorption. D. E. Paterson and S. J. Baker. J. Fac. Radiologists **9:** 183–194, October 1958. (Christian Medical College, Vellore, Madras, South India)

This communication records the radiographic findings in 51 patients in South India who were admitted for special investigations and were found to have malabsorption of essential foodstuffs (fat, sugar, or vitamin B_{12}), though no cause for this malabsorption, such as stricture, tumor, pancreatitis, jaundice, etc., could be found.

The patients were adults, chiefly of Indian nationality, of varied nutritional and social status. They usually complained of vague abdominal discomfort and mild chronic diarrhea. The radiographic signs were similar to those described in a wide variety of diseases and include the following:

(1) *Flocculation.* Flocculation assumed several forms (clumping, spiculation, granulation, a milky appearance). It is caused by the presence of mucus in the stool but may also occur with abnormal gastric or duodenal digestion, in the presence of bile-salts, or in the presence of short-chain fatty acids where there is rapid change of *p*H values.

(2) *Mucosal alterations.* Thick transverse folds were observed in the jejunum and ileum. Such thickening is also observed as a result of inflammatory changes secondary to acute enteritis, in infestation by parasites, and in nutritional and metabolic disturbances. The authors believe that in their cases the thickened jejunal folds may have been caused by

inflammation, edema, allergy, or abnormal conditions of the muscularis mucosae.

(3) *Motor disorders.* Increased caliber of the gut, irregular jerky peristaltic movements, segmentation of barium pattern, slow transit time, and the presence of gas in the small intestine, all indicate an abnormality of the neuromuscular mechanism in the submucous wall of the intestine.

The importance of distinguishing between constantly dilated loops of gut due to minor organic strictures and increased caliber due to motor disorder is stressed. Repeat examinations may be essential and laparotomy may be justified as a diagnostic final court of appeal in some cases. Ninety per cent of cases finally diagnosed as idiopathic malabsorption or sprue-like disorder showed positive radiographic signs.

Forty-five roentgenograms; 2 photographs; 1 chart.

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Radiological Demonstration of Variations in the Fluid Content of the Small Intestine During Dumping Attacks. E. Amdrup, Povl Hjorth, and J. Balslev Jørgensen. Brit. J. Radiol. **31:** 542–548, October 1958. (Copenhagen City Hospital, Denmark)

The authors studied the variations of the fluid content of the small intestine during dumping attacks. For this purpose they attempted to provoke such attacks by oral administration of 150 c.c. of 50 per cent glucose with barium. The subjects who exhibited symptoms of any account during this test fall into two main groups: (1) dumping patients and (2) patients with the "small-stomach" syndrome. The x-ray films afford an explanation of the two syndromes.

In patients with the dumping syndrome the ingested hypertonic solution was rapidly emptied from the stomach into the small intestine, where a pronounced binding of fluid took place, manifesting itself radiologically as dilution of the contrast medium. The dilution phenomenon was most pronounced at the time when the patients were feeling most miserable.

These findings appear to confirm the theory regarding the pathogenesis of the dumping syndrome, namely, a reduction in plasma volume. It is believed that the rapid gastric emptying with a spread of the hypertonic material over most of the small intestine gives rise to a transport of fluid from the blood stream to the intestinal tract to dilute the hypertonic solution. As a result, such large amounts of fluid may be bound in the small intestine that the dumping complaints are explicable as a consequence of a reduction in plasma volume.

In subjects with "small-stomach" symptoms there was no dilution in the small intestine. Instead, it took place in the gastric stump, giving rise to the distention which accounts for the local epigastric distress. The absence of systemic symptoms is evidently due to the fact that in these subjects the gastric function prevents a rapid emptying of the hypertonic fluid-binding material into the small intestine, the dilution taking place in a limited and, compared to the small intestine, quite small cavity.

The authors stress the importance of being able to distinguish radiologically between actual dumping and the "small-stomach" syndrome, since the operative repair of the two conditions differs.

Twenty roentgenograms; 2 graphs; 1 table.

THEODORE E. KEATS, M.D.
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Jejunal and Ileal Diverticulosis. Robert E. Lee and Nathaniel Finby. Arch. Int. Med. **102:** 97–102, July 1958. (R. E. L., 50 Popham Rd., Scarsdale, N. Y.)

Forty-five patients with diverticula of the mesenteric small intestine were studied at The New York Hospital in an effort to correlate the clinical and radiographic patterns of this condition. Meckel's diverticulum was excluded from the investigation since it represents a specific congenital diverticulum of the ileum as a remnant of the omphalomesenteric (vitelline) duct.

Diverticula of the mesenteric small intestine are usually acquired rather than congenital. They occur on the mesenteric border of the intestine, commonly at sites of vascular penetration of the mesenteric attachment. They are "false" diverticula, consisting of thin-walled sacs composed of mucosa, submucosa, and peritoneum. The muscle coats are markedly thinned or absent, and the diverticula are incorporated in the mesentery as rounded projections from the intestinal lumen. Size ranges from less than 1 cm. to over 10 cm. in diameter, with stomata of varying caliber. Usually the diverticula are multiple, but the number decreases distally. Thus, most diverticula are seen in the proximal jejunum; in the ileum they are rare.

The 45 patients in the present series consisted of 27 women and 18 men. Jejunal diverticula were found in 37 patients, ileal diverticula in 7, and both in 3 patients. Associated colonic diverticula were observed in 24 patients; of these, 10 also had duodenal diverticula and 1 had esophageal, duodenal, jejunal, and colonic diverticula.

Diverticula of the jejunum are commonly seen as large globular masses of barium density during routine radiography of the gastrointestinal tract. They may appear as pedunculated collections of barium continuous with the intestinal lumen or as residual round densities resembling "bunches of grapes" after emptying of the adjacent intestinal lumen. They may be multiloculated, oval, or round. They are usually smooth, without evidence of mucosal folds. If numerous, the diverticula may produce marked distortion of small intestinal motor function and simulate serious disease. In most instances they are incidental findings. Their chief radiologic interest lies in the field of differential diagnosis. In a roentgenogram of the abdomen diverticula may show air-fluid levels and simulate intestinal obstruction. Enteroliths within the diverticula may simulate biliary or renal calculi. Large diverticula may have the roentgen appearance of a tumor. During barium contrast study of the small intestine the uncomplicated diverticula may be confused with intrinsic inflammatory disease. Most diverticula of the ileum are seen in the terminal portion and thus can be distinguished from a Meckel's diverticulum.

Small intestinal diverticula tend to have wide necks and empty readily. Occasionally, however, delayed roentgenograms will show residual barium. Delay in emptying has been suggested as evidence of disease and may cause diagnostic difficulties.

Small diverticula of the small intestine may easily be missed unless careful scrutiny is combined with a high index of suspicion. Nonflocculating barium is advised as the contrast medium. Examination by barium meal should include films at thirty- to sixty-minute intervals until the entire small intestine is

visualized. Occasionally a barium enema study will demonstrate the terminal ileum to advantage.

Two cases showing uncommon complications (perforation, abscess, hemorrhage, and anemia) and a case in which a jejunal diverticulum simulated a marginal ulcer are reported.

Seven roentgenograms.

Malrotation of the Midgut in Infancy and Childhood. William B. Kiesewetter and John W. Smith. Arch. Surg. **77**: 483–490, October 1958. (Children's Hospital, Pittsburgh, Penna.)

The congenital abnormality termed malrotation of the midgut by the authors is perhaps better known to physicians as "malrotation of the colon." By "midgut" the embryologist refers to that portion of the gastrointestinal tract which is supplied by the superior mesenteric artery. It begins in the second portion of the duodenum and extends through the small intestine to a point in the midtransverse colon. The exact type of abnormality depends upon the stage at which the developmental process is arrested in fetal life.

In Stage 1, which includes up to the tenth week of fetal life, the midgut resides in the umbilical sac. Arrest during this period results in an omphalocele.

Stage 2 includes the tenth and eleventh weeks, during which the midgut is returned into the abdominal cavity and "rotation" occurs so as to arrange the bowel in the usual normal fashion except that at the termination of this stage the cecum is in the right upper quadrant. Arrest during this stage of development may result in a number of anomalies: (1) There may be complete nonrotation, with the small intestine on the right side of the abdomen and the colon on the left. The small bowel mesentery usually has no attachment to the posterior abdominal wall. (2) Duodenal obstruction, both acute and chronic, may result from peritoneal bands laid down by an incompletely rotated cecum placed in the midepigastrium. Obstruction secondary to volvulus of the incompletely rotated and incompletely immobilized midgut can, and often does, occur. (3) Ectopic fixation of the midgut may trap some coils of bowel and lead to an internal hernia.

During Stage 3, which includes the period from the twelfth week to birth, the cecum is thought to descend slowly into the right lower quadrant, and its mesentery to fuse to the posterior parietal peritoneum. Arrest during this stage may result in a subhepatic cecum, a retrocecal appendix, or the abnormally mobile volvulus-prone cecum.

Forty-four cases were studied by the authors, 80 per cent of the patients being under one month of age when they were seen with symptoms of obstruction manifested by acute or chronic vomiting. Older children may present with chronic intermittent abdominal symptoms associated with physical underdevelopment and malnutrition. Volvulus was associated in slightly less than half of the cases.

The decisive factor in diagnosis is the roentgenogram. The obstruction is most often due to a band at the second or third portion of the duodenum; therefore, the plain film shows gas within the stomach and proximal duodenum with absence or a paucity of gas beyond the ligament of Treitz. The point of obstruction and/or the abnormal position of the midgut can be confirmed by introducing contrast material into the stomach. Aqueous "Dionosil" has been used successfully for this purpose by the authors. A barium enema usually contributes little, since the crucial point is whether or not a high obstruction is present, not whether the colon is in an abnormal position. On occasion, pyloric stenosis, duodenal stenosis, annular pancreas, or reduplication of the duodenum will be impossible to differentiate on clinical and radiographic data alone.

Prompt and skilled surgery to release the obstructing bands, correct volvulus if present, and restore normal relations as much as possible is indicated. Surgeons are advised to inspect the entire midgut because of the frequency of associated anomalies, which are the usual cause of death. Thirty-two out of the forty-four patients in this series survived surgery and are presumed to be cured.

Seven tables. MAJ. MARTIN A. THOMAS, M.C.
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Chronic Ulcerative Colitis. I. Diagnostic Considerations. Nicholas C. Hightower, Jr., A. Compton Broders, Jr., Richard D. Haines, John F. McKenney, and Arno W. Sommer. Am. J. Digest. Dis. **3**: 722–733, October 1958. (Scott and White Clinic, Temple, Texas)

The authors discuss the diagnostic considerations in the problem of chronic ulcerative colitis based on experience with 220 proved cases seen at the Scott and White Clinic over the past fifteen years.

The diarrhea associated with chronic ulcerative colitis tends to be chronic and recurrent and frequently occurs nocturnally as well as in the daytime. Anorexia, weight loss, mild anxiety, tachycardia, fever, abdominal cramping, anemia, skin lesions, rectal complications, and joint involvement are the more common symptoms and signs. Important in the physical examination are auscultation and palpation of the abdomen and a careful digital examination of the rectum.

The diagnosis of chronic ulcerative colitis is dependent upon sigmoidoscopic and roentgenologic examination of the rectum and colon. The characteristic sigmoidoscopic findings vary with the stage and activity of the disease process.

Roentgen examination will reveal the extent of involvement of the colon, the degree of mucosal and luminal change, and the presence of complications. A properly conducted radiologic study starts with adequate preparation of the patient. It often is advisable to dispense with a preliminary laxative, but saline enemas are necessary to cleanse the lumen of the bowel. The examination must be done under fluoroscopic control, with a careful study of each segment of the colon as it fills with opaque medium.

Extreme irritability, as evidenced by spasm of the rectum and sigmoid as the barium enters this portion of the colon, is usually the first evidence of disease observed at fluoroscopic examination. This irritability may be present for some time before any other changes are demonstrable. When the disease process has reached the stage of ulceration, careful study of roentgenograms of the barium-filled colon will reveal changes in marginal detail. The clean-cut margins of the normal colon are replaced by some degree of irregularity. In the early stages, this may be merely a slight loss of a distinct margin. More severe ulcerative changes produce a feathery or a lacy margin or, as ulcerations become larger and more confluent, a markedly irregular, serrated border.

The mucosal pattern is best portrayed on roentgenograms made after the barium has been expelled, leaving only enough to coat the mucosa. Early stages of the disease cause loss of sharpness and blurring of mucosal detail. More severe ulcerative changes result in marked distortion or complete absence of the mucosal pattern. Double-contrast studies will reveal the presence of polyps or pseudopolypoid hyperplasia.

When the ulcerative process has existed long enough, alterations in the bowel wall occur, which distort the bowel lumen as observed roentgenologically. The wall changes consist of thickening and rigidity; one of the earliest luminal changes observed is loss of haustration. As the bowel is contracted by fibrosis and scarring, narrowing of the lumen and shortening of the entire colon may be observed.

Ulcerative colitis which involves the entire large bowel, including the cecum, usually results in a rigid, patulous ileocecal valve which offers no resistance to the flow of barium into the terminal ileum.

The authors discuss the differential diagnosis and list a number of diseases occurring in association with chronic ulcerative colitis.

Six roentgenograms; 4 photographs; 4 tables.

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Use of Barium Tannic Acid Enema in Investigation of Large Intestine. A. K. Bhattacharyya and D. E. Paterson. Indian J. Radiol. **12:** 59–67, May 1958. (Christian Medical College Hospital, Vellore, India)

The authors have routinely utilized a mixture of tannic acid and barium in 614 barium enemas. They use 0.5 gm. of tannic acid powder per 100 c.c. of barium suspension. Routine films are made in the filled state, after evacuation, and after introduction of air.

The incidence of good contraction of the bowel following evacuation rose from 37 to 81 per cent after the introduction of tannic acid. It is felt that this substance promotes adherence of barium to the colonic wall during the air-contrast study.

The incidence of various disease in the 614 patients is tabulated and it is of some interest that almost 9 per cent had tuberculosis. Slightly less than 11 per cent had colitis of unspecified etiology; only 6 per cent had carcinoma.

Ten roentgenograms; 2 tables.

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Remarks on the Clinical and Radiologic Diagnosis of Meckel's Diverticulum. Report of a Case. Morris C. Miller. Gastroenterology **35:** 414–417, October 1958. (Jewish General Hospital, Montreal, Que., Canada)

The author reports a case of Meckel's diverticulum diagnosed clinically and confirmed by x-ray examination prior to surgery. The patient was a twenty-three-year-old male who complained of dull throbbing pain in the right upper abdomen, occurring usually one hour after lunch and disappearing spontaneously. Antacids and milk had no effect on the symptoms. Stools were positive for blood. On a barium enema study the ileum was filled, and the post-evacuation film showed no abnormalities. Fluoroscopy and spot films, however, demonstrated the diverticulum. The author advises this technic rather than a small bowel series for demonstrating Meckel's diverticulum. Most patients will show filling of the ileum by reflux of barium during a barium enema study.

Four roentgenograms.

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Toledo, Ohio

Changes in the Gallbladder After Elective Gastric Surgery. H. T. Cox, J. F. Doherty, and D. F. Kerr. Lancet **1:** 764–766, April 12, 1958. (Wythenshawe Hospital, Manchester, England)

An investigation has been made of the behavior of the gallbladder, especially after a fatty meal, in 18 patients before and after elective gastric surgery. The surgery performed was partial gastrectomy (Billroth II), 9 cases; partial gastrectomy (Schoemaker), 2 cases; partial gastrectomy and vagotomy, 4 cases; vagotomy and posterior gastroenterostomy, 3 cases. The contrast medium employed for intravenous cholecystography was Biligrafin. One series of films (the immediate preoperative) was taken within twelve days before operation; the second (the immediate postoperative) within twelve days after operation, and the third (the late postoperative) after an interval of not less than six months. A series of films consisted of a two-hour fasting film showing the size and position of the gallbladder, followed by six films showing the rate of emptying after a glass of hot milk with an egg. In some patients only two series of films were taken because of the potential danger of excessive radiation.

In 15 cases there was a preoperative series of films followed by at least one postoperative series. In 14 of these the gallbladder became very much dilated. It can be said, therefore, that dilatation of the gallbladder is an almost consistent change after elective gastric surgery. In some cases the volume had doubled. The authors consider this doubling in the volume of the gallbladder in twelve days after simple gastrectomy one of the most striking concomitant physiological changes seen in all abdominal surgery.

In 11 cases the emptying rate of the gallbladder was increased after a fatty meal. This increase was mainly limited to the ten-minute and fifteen-minute films, showing that emptying begins earlier and is more active than before operation. Dilatation of the gallbladder and increase in emptying rate must be accepted as unrelated changes, because not all the gallbladders that were dilated showed an increase in emptying rate, and the emptying rate was increased in undilated gallbladders. No film revealed dilatation of the common duct, either at the time of dilatation or emptying of the gallbladder. There was therefore no indication at any time of contraction or failure of relaxation of the sphincter at the lower end of the common duct.

In 2 cases the gallbladder had apparently moved downward, by the width of one lumbar vertebra.

The authors believe that the gallbladder dilatation is probably caused by section of the vagus nerves, and that the emptying rate of the gallbladder probably depends on that of the stomach.

Five roentgenograms; 1 table.

Biligrafin and the Non-Visualized Gall-Bladder. David Stenhouse. J. Fac. Radiologists **9:** 223–225, October 1958. (Western Infirmary, Glasgow, Scotland)

This paper is concerned with the use of Biligrafin for intravenous cholegraphy when oral cholecystography has failed to outline the gallbladder.

The preparation used is Biligrafin Forte, the dose being 20 c.c. Films of the gallbladder area are taken and viewed wet at intervals of twenty, forty, sixty, and ninety minutes after the injection. If the gallbladder is not visualized on any of these films, the decision as to whether to take more has been found by experience to depend on the appearance of the bile ducts. If these are clearly demonstrated on the films taken up to ninety minutes, there is no point in continuing, since the gallbladder will not show up later. On the other hand, if the ducts in the early films are seen faintly or not at all, the gallbladder will occasionally appear on films taken at any time up to five or six hours after the injection.

In the period under review Telepaque had failed to outline the gallbladder in a total of 129 cases, and Biligrafin was then given. With this medium the gallbladder was demonstrated in 26 cases, the bile ducts but not the gallbladder in 85 cases, and neither in 18 cases.

The author concludes that the oral method of cholegraphy using a medium such as Telepaque makes it possible in the majority of cases referred for radiological examination of the gallbladder to give a positive opinion as to whether or not the gallbladder is diseased. The method fails when the gallbladder is not visualized. It is impossible to say in a given case whether the failure of visualization is due to gallbladder disease or to some other factor such as malabsorption or hepatic dysfunction. By carrying out intravenous cholegraphy with Biligrafin, this doubt can be removed, according to the present study, in no less than 82 per cent of the cases examined. With the exception of the jaundiced case in which the serum-bilirubin level is greater than 4 mg./100 c.c., failure of visualization of the gallbladder after an oral opaque medium is therefore a definite indication for the use of Biligrafin.

One table. THEODORE E. KEATS, M.D.
University of Missouri

Syndrome of the Cystic Duct. F. Raboni. Ann. di radiol. diag. **31:** 338–353, 1958. (In Italian) (Instituto di Radiologia e del Radium dell'Università di Parma, Italy)

When peroral cholecystography fails to reveal gallstones, the patient is usually maintained under conservative medical management. If there is no relief of subjective (pain, dyspepsia) or objective (spot-tenderness, icterus) symptoms, while at the same time the opacified gallbladder cannot be stimulated by a fatty meal, surgical exploration is often recommended. Injection of the contrast material into the cystic duct (which appears to be narrower than usual), in peroperative cholangiography may be attended with difficulty, and there is often a distended, flabby gallbladder. Under these circumstances, even in the absence of palpable stones, cholecystectomy is indicated. In the 8 illustrative observations included in this paper, removal of the gallbladder resulted in apparently lasting cure. Histologic examination of the surgical specimens revealed fibrosis of the stenotic cystic duct, in many cases with desquamation of the lining epithelium. This novel nosologic entity, appropriately labeled *syndrome of the cystic duct*, provides an excellent justification for cholecystectomy in the absence of demonstrable cholelithiasis.

Fifteen roentgenograms. E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Biliary Vesicular Stasis. J. Dudfield Rose. Lancet **1:** 1356–1360, June 28, 1958. (Royal Victoria Infirmary, Newcastle-upon-Tyne, England)

The most common disorder of the biliary tract is one of motility, namely, biliary dyskinesia. It was found, either alone or in association with some morphological change, in 126 of 200 consecutive cases investigated and treated for some biliary-tract disorder by the author. The simplest and commonest form of dyskinesia is a vesicular stasis, in which the gallbladder empties insufficiently. This was present in 34 of the 126 cases of dyskinesia in the author's series. Biliary vesicular stasis may be hypotonic or hypertonic.

Hypotonic vesicular stasis (20 cases): Hypotonic vesicular stasis is a slowly progressive disease, occasionally with exacerbations. It is more common in women and usually begins early in life. The patient complains of a heavy, dull feeling in the epigastrium and below the right costal margin, which comes on a quarter to half an hour after meals and remains for two to three hours. There may be tenderness on palpation below the right costal margin. On cholecystography, the gallbladder often appears long and flask-shaped, lying parallel to the spinal column. In the erect position, the density of the shadow is greatest in the fundus. An accurate diagnosis is possible only by serial cholecystography (Rose: Brit. M. J. **1:** 360, 1958. Abst. in Radiology **71:** 898, 1958), in which a series of films (anteroposterior and lateral) are taken before and at ten-minute intervals after a fatty meal. From these the volume of the gallbladder is computed and an evacuation curve is drawn. The angle which the long axis of the gallbladder makes with the spine in the lateral view (angle of erection) is measured; the size of this angle is an indication of the tone and the degree of contraction of the gallbladder. On serial cholecystograms the cystic duct is often visible before the fatty meal is given, the gallbladder is seen to evacuate insufficiently at all stages, and there is little or no evidence of active contraction or tone.

It may be impossible to distinguish between a primary and a secondary stasis before operation and manometric investigation (apart from trans-parieto-hepatic vesicular puncture). The peroperative investigations are (1) measurement of the pressure within the biliary tract on a recording manometer and (2) radiography of the biliary tract after the injection of Diodone. Peroperative radiography shows the distended, elongated, flask-shaped gallbladder. It evacuates easily into the common duct, which is itself hypotonic, and the opaque material flows without resistance into the duodenum and also up into the hepatic ducts. The sphincter of Oddi is widely open. The common duct is usually widely dilated and evacuates rapidly; the hepatic duct may also be dilated. The hepatic and common ducts often form part of a large curve, or they may be sinuous.

Hypertonic vesicular stasis (14 cases): In hypertonic vesicular stasis the gallbladder empties insufficiently because of some obstruction, either functional or mechanical. The intravesicular pressure is raised when it is measured by manometry at operation. The purely functional type is quite rare; there were only 5 examples in the author's series. This condition is caused by spasm of the sphincter of Lütkens, and may be associated also with spasm of the sphincter of Oddi. Serial cholecystograms show a vesicular

stasis with increased vesicular tone. In longstanding cases a hyposystole may be present, *i.e.*, a slight initial contraction of the gallbladder, which, however, soon passes off.

A hypertonic vesicular stenosis may be caused by a valve-like abnormality in the region of the junction between the cystic duct and the gallbladder. These valve-like peculiarities and certain dysplasias of the neck of the gallbladder and infundibulum give rise to intermittent obstruction to gallbladder evacuation, which is followed by dilatation, angulation, and further obstruction. The clinical signs and symptoms and the cholecystographic findings are variable and depend on whether the gallbladder is able to contract forcibly against the obstruction or whether contractile power has failed and a state of atony exists. In the early stages of this condition the serial cholecystogram shows a gallbladder which evacuates insufficiently, with an increase in tone and contraction. In most cases there is an obvious kink in the infundibulo-colic region, usually best seen in the lateral views, but sometimes more distinctly visualized in the anteroposterior view. Eventually the gallbladder loses its power to contract effectively against the obstruction. In this late stage cholecystograms show the gallbladder to be atonic, and it is possible to differentiate this condition from a primary hypotonic stasis only at operation. In the present series there were 6 patients with a valve or kink, 1 associated with a gallstone.

Eventually in most cases of biliary vesicular stasis there must be recourse to surgery. Of the author's 34 cases treated surgically, the results were good in 31, only 3 remaining unimproved.

Eight illustrations, including 5 roentgenograms; 3 tables.

The Developmental Basis for Bile Duct Anomalies. Mark A. Hayes, Ira S. Goldenberg, and Courtney C. Bishop. Surg., Gynec. & Obst. **107:** 447–456, October 1958. (Yale University School of Medicine, New Haven, Conn.)

Sporadic cadaver and autopsy studies, supplemented by clinical and radiologic observations, have emphasized the variability that is to be found in the configuration of the biliary duct pattern. The present report is concerned with the embryologic basis for the anomalies encountered during operation in a consecutive series of 400 primary operations on the biliary tract. By careful examination at the time of operation and by operative and postoperative cholangiography, 189 significant anomalies were discovered, an incidence of 47.25 per cent. The authors have classified these anomalies as follows:

Type I: Accessory Ducts (72 cases):
- (*a*) Cystohepatic
- (*b*) Cholecystohepatic (the most commonly encountered)
- (*c*) Choledochohepatic, low
- (*d*) Choledochohepatic, high
- (*e*) Double choledochohepatic

Type II: Anomalous length of common hepatic duct (104 cases):
- (*a*) High junction of cystic with common hepatic duct (trifurcation)
- (*b*) Low junction of cystic with common hepatic duct (the most commonly encountered)

Type III: Anomalous junction of cystic with common hepatic duct (11 cases)
- (*a*) Posterior
- (*b*) Left hepatic duct
- (*c*) Left side-cross anterior (the most commonly encountered)
- (*d*) Left side-cross posterior
- (*e*) Double wind
- (*f*) Mucosal septum only
- (*g*) Absent cystic duct

Type IV: Anomaly of common duct (2 cases)
- (*a*) Diverticulum of common duct
- (*b*) Common duct emptying into duodenal diverticulum

Types I and II account for 44 per cent of the patients operated upon and 93.11 per cent of the anomalies found.

The authors describe the various anomalies and illustrate them by cholangiographic studies and sketches.

Nine roentgenograms; 18 diagrams; 1 table.

MIGUEL CHIAPPORI, M.D.
University of Pennsylvania

Cholecystocholangiography with Cholecystokinin. A. J. Ch. Haex and D. Limburg. J. belge de radiol. **41:** 429–445, 1958. (In Dutch) (Academisch Ziekenhuis te Leiden, The Netherlands)

Cholecystokinin, a duodenal hormone considered to be responsible for contraction of the gallbladder, was discovered in 1928 by Ivy and Oldberg. In 1956 a pure and concentrated form was obtained by Jorpes and his collaborators. The authors used this substance in cholangiographic examination in 27 patients. One to two minutes after the intravenous injection of cholecystokinin, there is usually a strong contraction of the gallbladder, and the maximum contraction occurs after ten to fifteen minutes.

There was good visualization of the major bile ducts if the gallbladder were sufficiently opacified prior to injection. It is quite possible that this procedure will replace the fatty meal for gallbladder work.

It is postulated that the successive administration of cholecystokinin and of secretin, which stimulates flow of pancreatic juice, may offer the possibility of obtaining separately bile and pancreatic juice through a duodenal tube.

Twenty-one roentgenograms; 1 table.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Clinical and Surgical Aspects of Pancreatic Pseudocyst; Analysis of Fifty-eight Cases. John M. Waugh and Thomas E. Lynn. Arch. Surg. **77:** 47–54, July 1958. (Mayo Clinic, Rochester, Minn.)

A cyst surrounded by a sac which does not have an epithelial lining is commonly referred to as a "pseudocyst," in contrast to a true cyst. The authors have found this one of the commonest types of cyst associated with the pancreas. Fifty-eight cases were encountered at the Mayo Clinic from 1948 through 1954.

Of the 58 patients, 35 were men; 48 were between the ages of thirty and sixty. Inflammation and trauma seemed to be the predisposing factors. Fifteen patients were found to have acute or subacute pancreatitis at surgery and an additional 6 had a preoperative diagnosis of acute pancreatitis. Thirty-seven patients had

histories of recurrent acute pancreatitis and 12 were found to have biliary disease at surgery. Eleven patients gave a history of excessive alcohol intake over a long period. Six related the onset of symptoms to an episode of severe trauma to the abdomen.

The chief symptom is pain, typical of pancreatitis. Jaundice and vomiting also occur, and 6 patients in the authors' series showed evidence of high intestinal obstruction. In 35 cases there was a palpable mass in the upper portion of the abdomen.

Radiographic studies may reveal significant evidence of pancreatic disease—an upper abdominal mass or evidence of calcification in the region of the pancreas. The duodenal loop may be widened and the stomach may be displaced or indented by the cyst. Pressure of the cyst may impede the gastric emptying. External drainage is the treatment of choice but internal drainage may be indicated in selected cases.

Five roentgenograms. GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

THE DIAPHRAGM

Problem of the Ruptured Diaphragm. Philip E. Bernatz, Alfred F. Burnside, Jr., and O. Theron Clagett. J.A.M.A. **168:** 877–881, Oct. 18, 1958. (Mayo Clinic, Rochester, Minn.)

A series of 112 patients undergoing surgical repair of a ruptured diaphragm is reported. None had a hernial sac, and hiatus hernia was not included. Of these ruptures, 70 per cent were secondary to automobile accidents. The average age was thirty-five years. Males were predominant, 9 to 2. The left side was ruptured in 104 cases, the right in only 8. There were no bilateral ruptures in the series. Transthoracic repair is recommended, as soon as the patient's condition permits.

Only a few patients (6) had severe, life-endangering problems secondary to the rupture immediately after the trauma, but associated severe injuries were common. The largest group of patients had prolonged rather mild complaints leading to eventual diagnosis. The average interval between trauma and diagnosis was four and a half years. Some (9) of the series were diagnosed with acute complicating obstruction after prolonged complaints. Some (4) were asymptomatic.

Chest roentgenograms were frequently interpreted as showing eventration of the diaphragm. A high index of suspicion is necessary to avoid error. Extraneous shadows above the diaphragm, such as gas-containing or homogenous areas, with mediastinal shift to the other side, is suggestive. The omentum is the structure most commonly traversing the rent, but it is usually accompanied by a portion of the stomach or colon. There is occasional lung collapse adjacent to the rupture. Contrast ingestion is diagnostic but may be contraindicated in acutely ill patients with obstruction.

Five roentgenograms. B. JAY HILL, M.D.
University of Michigan

THE MUSCULOSKELETAL SYSTEM

Haemoglobin SC Disease. W. P. Cockshott. J. Fac. Radiologists **9:** 211–216, October 1958. (University College Hospital, Ibadan, Nigeria)

On the basis of 20 cases from West Africa, the author discusses the clinical features and radiographic findings in hemoglobin SC disease.

The occurrence of the sickling phenomenon in red blood corpuscles has been known for several decades, but it is only in recent years that the various clinical entities associated with sickling have been recognized as distinct. In 1950 a new hemoglobin in a North American Negro was described and this was named C hemoglobin (Itano and Neel: Proc. Nat. Acad. Sci. **36:** 613, 1950). It may exist in a homozygous form or as a carrier trait. As a carrier trait hemoglobin C gives rise to no clinical abnormality. However, when hemoglobin C is conjoined with hemoglobin S, there is produced a definite entity which is termed hemoglobin SC disease. In contrast to the widespread distribution of the sickle-cell gene, the hemoglobin C gene appears to have originated from a focus in Northern Ghana and to have spread from there to all sides, with gradually declining frequencies of the C gene. Sporadic examples of hemoglobin C found in Algeria, South Africa, the Congo, the West Indies, and in the United States are the result of the migration of West African slaves.

In hemoglobin SC disease bone infection is very frequent. Radiologically, slight but significant changes in bone texture of the skull and long bones are noted in about one-third of the patients. These are not related to age or degree of anemia. Avascular joint changes are present in one-third of the cases, the hips and shoulders being most frequently involved. The avascular process is multifocal, discrete, and subchondral. The process is analogous to that occurring in caisson disease. The hip lesions differ from classical Perthes' disease as they are subchondral, focal, and perhaps multicentric, in contrast to massive involvement of the whole capital femoral epiphysis. In SC disease the femoral neck and metaphysis are spared.

Fourteen roentgenograms.

THEODORE E. KEATS, M.D.
University of Missouri

Osteopoikilosis. A Case Report. R. Uebelhart, W. Hinderling, and W. Voellmy. Schweiz. med. Wchnschr. **88:** 93–95, Jan. 25, 1958. (In German) (Bezirksspital, Langenthal, Switzerland)

The authors report a case of osteopoikilosis in an obese 24-year-old male. Clinically the patient presented a picture simulating an endocrine disturbance of the Cushing type, while roentgenologically the bone changes indicated osteopoikilosis. Small areas of sclerosis involved the carpal bones, the metacarpals, and phalanges of the hands, and many of the other bones except the skull. A trochanter biopsy showed a heavy spongiosa within which were smooth, star-shaped, well circumscribed solid bone trabeculae, to the size of 2 mm. Superficially these trabeculae were heavy; in the deeper layers they were slender. Fatty bone marrow filled the marrow spaces.

The authors agree with Schmorl that osteopoikilosis is a congenital condition, and occasionally familial. The histologic findings in the case presented agree with those previously described by Schmorl (Fortschr. a. d. Geb. d. Röntgenstrahlen **44:** 1, 1931. Abst. in Radiology **17:** 1078, 1931).

Three roentgenograms; 1 photomicrograph.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

The Marfan Syndrome, with Special Reference to Congenital Enlargement of the Spinal Canal. J. D. Nelson. Brit. J. Radio. **31:** 561–564, October 1958. (Western Infirmary, Glasgow, Scotland)

The author reviews the literature on the Marfan syndrome and reports 4 new cases which showed congenital enlargement of the spinal canal. None of the patients presented any neurological abnormalities, and the enlargement was of a haphazard nature, involving depth, width, or both. Spinal canal enlargement produces typical bone changes, namely, narrowing of the pedicles, widening of the interpedicular distances, and posterior scalloping of the vertebral bodies.

In this syndrome other spinal defects are encountered, including spina bifida, congenital fusion, alteration in the shape of the vertebral bodies, and underdevelopment of a spinous process. The presence of the intact cortex on the posterior aspects of those vertebral bodies showing scalloping and also that covering the narrowed pedicles indicate that these effects are not caused by an expanding lesion.

The fact that the patients reached adult life without the appearance of neurological abnormalities indicates that there is no underlying diastematomyelia. Differentiation from other causes of spinal canal enlargement is easy because of the presence of other stigmata of the syndrome and absence of neurological manifestations.

Six roentgenograms; 2 photographs.

THEODORE E. KEATS, M.D.
University of Missouri

Lumbar Extradural Cysts—Congenital: Their Proper Classification. George W. Smith and Marcelino Chavez. Arch Neurol. & Psychiat. **80:** 436–440, October 1958. (Division of Neurological Surgery, The Medical College of Georgia, Augusta, Ga.)

Congenital extradural spinal cysts are very rare, with only 35 cases reported in the medical literature. They usually occur in the dorsal area, sometimes extending into the lumbar region. Only 2 of the recorded cases were limited to the lumbar area. The pathogenesis is that of a small defect in the dura mater through which the arachnoid membrane, containing cerebrospinal fluid, herniates. The symptoms and signs are those of spinal cord compression, not unlike those incident to disk herniation.

The x-ray findings may be erosion of the pedicles with increase of the interpedicular distance and erosion of the posterior margin of the vertebral body (on the side opposite the cyst if the latter is in the lumbar region). Myelography will outline the cyst with Pantopaque.

A case report of a lumbar extradural cyst is given with review of the literature. The difference in clinical behavior between lumbar and spinal (thoracic) cysts is discussed.

Two roentgenograms; 4 diagrams; 1 table.

J. S. ARAJ, M.D.
Toledo, Ohio

Different Stages of Radiological Epiphyseal Union. I. D. Bajaj. Indian J. Radiol. **12:** 70–73, May 1958. (Lady Hardinge Medical College, New Delhi, India)

Appearance of the epiphyses at the knee and ankle was studied in 6 groups of 50 males, each, between fifteen and twenty years of age. Union of the epiphysis is divided into six stages, illustrated by simple line drawings In the first stage there is no evidence for union and the ossification center is seen separated from the shaft. In the second stage there is capping of the shaft by the epiphyseal ossification center, with no change in the diaphyseo-epiphyseal space. In the third stage beginning union of the epiphysis to the shaft is demonstrated by transverse wavy lines. The fourth, fifth, and sixth stages are different phases of union. In the fourth there is still some notching where complete union has not occurred. In the fifth stage there is complete union, and in the sixth stage the line of sclerosis occurs in the area of the plate. A very brief review of some of the literature regarding epiphyseal closure is included.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

Observations of Neuropathic (Charcot) Joints Occurring in Diabetes Mellitus. Julian E. Jacobs. J. Bone & Joint Surg. **40-A:** 1043–1057, October 1958. (123 W. 7th St., Charlotte 2, N. C.)

Three cases of diabetic neuropathic arthropathy involving the foot and ankle are reported and the literature concerning this entity is reviewed.

In 2 of the 3 cases, serial roentgen studies of the feet and ankles revealed pathological fractures, progressive bone destruction with fragmentation, and subluxations. Both patients had continued walking with little or no pain despite the severe bony changes. In the remaining case, initial roentgenograms of the feet revealed pathological fractures of the metatarsals with fragmentation involving joint surfaces. The patient's diabetes was well controlled and there was no evidence of vascular insufficiency or infection. Vibratory sensations were absent in both ankles and feet, patellar reflexes were diminished and ankle reflexes absent. Antibiotics were administered and roentgen therapy was directed to the foot because of a clinical impression of low-grade osteomyelitis. Biopsy, however, disclosed necrosis but no evidence of osteomyelitis. One year later, roentgenograms showed improvement in the fractures and the patient was able to walk without discomfort. Nine years later, roentgenograms revealed complete healing of the involved bones. Apparently, this is the first recorded case of healing of a neuropathic joint.

The 3 cases reported here bring the total cases in the world literature to 45 (1956).

Thirty-one roentgenograms; 1 photomicrograph; 2 photographs.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

Anteroposterior Projection of the Carpometacarpal Joint of the Thumb by Radial Shift of the Carpal Tunnel View. Michael Burman. J. Bone & Joint Surg. **40-A:** 1156–1157, October 1958. (130 East 67th St., New York 21, N. Y.)

An anteroposterior projection of the greater multangular-first metacarpal articulation is described. The hand and wrist are positioned for an ordinary carpal tunnel view, the tube is angled approximately 45°, and the central ray is directed toward the radial aspect of the proximal hand. The joint in question is distorted by magnification and its outline is concavo-convex. The projection described better demonstrates the carpometacarpal joint of the thumb than the

routine anteroposterior and lateral views of the wrist.

Two roentgenograms; 2 photographs.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

GYNECOLOGY AND OBSTETRICS

The Roentgenologic Interpretation and Uses of Percutaneous Retrograde Pelvic Arteriography. Billy P. Sammons, John R. Williams, Charles Gartenlaub, Richard L. Bernstine, James H. Nelson, Jr., and Robert B. Greeman. Am. J. Roentgenol. **80:** 664–672, October 1958. (United States Naval Hospital, St. Albans 25, Long Island, N. Y.)

The technic used by the authors for delineation of the uterine arteries is described in detail. Miokon (50 per cent) is used as the contrast medium. After insertion of a cannula into one of the femoral arteries inferior to the inguinal ligament, pressure cuffs are applied to the lower extremities and inflated well above the systolic pressure. The contrast material is injected rapidly (20 c.c. in obstetric cases and 30 c.c. in gynecologic cases) and roentgenograms are obtained at proper intervals. In obstetrical problems, one anteroposterior roentgenogram is made three seconds after completion of the injection. In gynecological problems a serialograph is used and six roentgenograms are made at one-second intervals beginning halfway through the injection.

The authors have had no serious complications in a series of 85 patients, including 45 pregnant women, representing all trimesters.

This procedure may be of great value in suspected cases of placenta praevia. The placental sinuses can be visualized in the third month. In tubal pregnancy, positive diagnostic findings may be demonstrated at the end of the second month. Uterine fibromyomata may be shown and determination of the cause of uterine bleeding may be facilitated by study of the uterine myometrial vasculature.

Retrograde femoral arteriography should be considered when simpler and safer procedures have failed to give necessary information and when the results of the examination might reasonably be expected to have a bearing on the choice between radical and conservative therapy.

Ten roentgenograms; 1 diagram; 3 tables.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

A Hysterographic Study of Uteri After Caesarean Section. L. O. S. Poidevin and V. Y. Bockner. J. Obst. & Gynaec. Brit. Emp. **65:** 278–283, April 1958. (University of Adelaide, Adelaide, Australia)

The authors report a hysterographic study of 56 patients who were delivered in 1952 or subsequently at the Queen Victoria Maternity Hospital, Adelaide. Thirteen of the women had had vaginal deliveries and 43 had been delivered by cesarean section. The group of 43 is further subdivided into those who had one cesarean section (26), those who had more than one cesarean section (10), those who had a vaginal delivery subsequent to cesarean section (5), and those who had a delivery following the hysterographic examination (2). The time-interval between the cesarean section and hysterography exceeded six months in most instances.

In the hysterograms of all of the 13 control cases, the uterus had a smooth regular outline. Every uterus which had been subjected to previous cesarean section showed some degree of deformity. The deformities were arbitrarily divided into small and large, depending on whether they were above or below 5 mm. in depth. In 27 cases the scars were considered small and in 11 large. Five cases were not classified. The authors believe that the deformities demonstrated occur at the site of the uterine incision. No relationship was established between the size of the deformity and the variable clinical factors, such as age, parity, indication for cesarean section, time in labor, operative technic, postoperative pyrexia, wound healing, or time of x-ray examination.

The authors recommend that a repeat cesarean section be performed in any woman with a large uterine deformity.

The practicability of x-ray examinations of the uterus after cesarean section may be increased by selection of cases after further studies have been done. The procedure is risk-free except as it involves an extra exposure to radiation.

Twelve roentgenograms; 1 photomicrograph; 1 photograph.

Complications of Hysterosalpingography. John H. E. Woltz, W. Z. Bradford, W. B. Bradford, and Joseph B. McCoy, Jr. Am. J. Obst. & Gynec. **76:** 736–741, October 1958. (Bradford Clinic, Charlotte, N. C.)

The complications encountered in obtaining 500 consecutive hysterosalpingograms on private white patients were: pain in 14 patients, shock-like syndrome in 9, pelvic infection in 5, vaginal bleeding in 3, and intravasation of the opaque material into the venous channels in 6 patients. There was no death and very little morbidity. Serious infectious complications have been more frequent with the Rubin test.

The studies in which these observations were made were performed ten to thirteen days after the onset of menstruation, without anesthesia; a multiple injection technic without fluoroscopy was used. Iodochlorol was the radiopaque medium. Precautions were taken to perform the procedure with the patient's stomach empty, to limit the examination to women without known pelvic infection, and to discontinue the injection upon the first sign of complication.

Six tables.

ROBERT L. EGAN, M.D.
University of Texas, Houston

One Radiograph to Exclude Placenta Prævia. Albert A. Earn, J. L. Freer, and D. R. Cairns. Lancet **1:** 828–829, April 19, 1958. (A. A. E., 414 Atlantic Ave., Winnipeg 4, Manitoba, Canada)

The authors have investigated the accuracy and practical value of a single lateral radiograph of the uterus in 107 cases of suspected placenta praevia. Indications for roentgen examination were antepartum hemorrhage, malpresentation, unstable lie, or high fetal head. The apparatus consisted of a standard four-valve x-ray unit with a rotating anode tube and tilting table. Three radiographs were taken routinely in each case. These were a lateral view of the uterus, the pelvis in the erect position, and the pelvis in the semierect position. A wedge filter was not employed. The films were read on a standard viewing box. Separate illumination by a 100-watt bulb was necessary for viewing the anterior aspect of the uterus and adjacent abdominal wall.

The placenta was correctly identified in the upper uterine segment in 90 of the 107 cases. At the beginning of the investigation, the placenta in 1 case was wrongly interpreted as entirely in the upper segment; examination under anesthesia revealed a second-degree anterior placenta praevia. With soft-tissue and displacement radiographic technics, placenta praevia was missed in 3 cases and correctly diagnosed in 12; radiographic findings were inconclusive in 2 cases. It was observed that, if there was no placental shadow in the upper uterine segment, placenta praevia was likely to be found clinically.

The most significant conclusion reached was that radiological localization of the placenta in the upper uterine segment is highly accurate; a lateral radiograph of the uterus taken after thirty-four weeks gestation, in the absence of hydramnios, yielded the necessary information to exclude placenta praevia. One such radiograph is compatible with good obstetric standards; irradiation to fetus and mother is minimal; film costs are reduced; and fetal abnormalities may also be detected.

The Cervical Canal and Abortion. W. J. Rawlings. M. J. Australia **2:** 487–489, Oct. 11, 1958. (Royal Women's Hospital, Melbourne, Australia)

Patients with repeated abortions should undergo hysterography to exclude abnormalities of the uterine body and cervical canal. The author places considerable significance on the width of the cervical canal. His film measurements are corrected for magnification and correlated with the outcome of subsequent pregnancies in 24 patients with histories of earlier abortions. According to cervical canal width, the series was divided into two groups, the first, in which the canal measured up to 6 mm., and the second, in which it exceeded 6 mm. In Group I it was found that hormone treatment, with correction of decidual failure, resulted in considerable increase of the number of mature pregnancies. In Group II hormone treatment had some good results as to number of mature pregnancies, though not comparable to Group I.

The author's conclusion from this small series is that in cases of small cervical canal the abortion is due to decidual failure, while the patient with a dilated cervix is prone to abort even when the pregnanediol excretion is normal.

Four roentgenograms; 2 tables.

J. S. ARAJ, M.D.
Toledo, Ohio

The Prenatal Roentgen Diagnosis of Fetal Hydrops. Eugene M. Savignac. Am. J. Roentgenol. **80:** 673–680, October 1958. (Holy Cross Hospital, Detroit 34, Mich.)

Erythroblastosis fetalis has been subdivided into three groups clinically. They are: (1) congenital anemia, (2) icterus gravis neonatorum, and (3) fetal hydrops. Congenital anemia is the mildest form and is usually self limited. Icterus gravis neonatorum is by far the most common form and is manifest by jaundice and progressive anemia with numerous nucleated red blood cells. Fetal hydrops, the most serious type of erythroblastosis fetalis, is almost universally fatal during the last trimester of pregnancy. Rarely, the fetus may be born alive and succumb within a few hours. The condition is manifested by severe generalized edema of the subcutaneous tissues and the internal organs of the fetus and by edema of the placenta.

The significant roentgen findings are:

(1) *A dead fetus* in the last trimester of pregnancy with the usual signs of fetal death.

(2) *Edema of the fetus.* Normally, the fetus shows a layer of subcutaneous fat outlining the contour of the body and the extremities. This fat line becomes invisible because of infiltration of the fatty tissue by edema fluid.

(3) *Evidence of a large placenta.* The placenta will occupy almost half of the volume of the uterine cavity and must necessarily displace the fetus to either a lateral, anterior, or posterior margin of the uterus.

(4) *Abnormal attitude of the fetus.* The severe edema of the soft tissues of the neck, chest, and abdomen produce a straightening of the entire trunk and the neck of the fetus. Also, as a result of edema of the extremities, the arms and legs are no longer flexed but tend to project at right angles to the trunk. This has been described as the "Buddha sign."

Four case reports with illustrative roentgenograms are presented.

Nine roentgenograms; 1 photograph.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

Intravascular Gas in the Radiological Diagnosis of Foetal Death in Utero. Paul Ross. M. J. Australia **2:** 495–497, Oct. 11, 1958. (Melbourne, Australia)

The author reports a case of fetal death diagnosed *in utero* by the presence of intravascular gas. This sign of fetal death was first described in 1944 by Roberts (Am. J. Roentgenol. **51:** 631, 1944) and 48 cases are said to have been recorded up to the present time. To these another is now added. Gas has been shown in the vessels of the head and neck, the heart and lungs, the abdomen, the extremities, and the umbilical cord. The most characteristic appearances are the rounded lobulated shadows made by gas in the heart and the tree-like shadow of gas in the hepatic vessels.

The incidence of intravascular gas in fetal death is not definitely known, because of the small number of cases, but is estimated to be about 50 per cent. Holm (Acta obstet. et gynec. scandinav. **36:** 58, 1957) found intravascular gas after birth in 20 of 29 fetuses which had died *in utero* before commencement of labor. Of these, 22 were examined radiographically during pregnancy, and gas in the fetal circulatory system was demonstrated in 12 cases.

Unlike Spalding's sign (overlapping of the bones of the vault of the skull) the presence of intravascular gas is an absolute indication of fetal death. The gas appears about three or four days after death and will remain demonstrable for at least two weeks. Spalding's sign is usually of later occurrence. The roentgenograms should be made in the anteroposterior (recumbent) and lateral (upright) projections.

The origin of the gas is not definitely known. The author mentions the various theories offered in the literature.

Four roentgenograms.

J. S. ARAJ, M.D.
Toledo, Ohio

Deuel's Halo Sign. Olov Fr. Holm. Am. J. Roentgenol. **80:** 681–683, October 1958. (Länslasarettet, Falköping, Sweden)

On roentgen examination of mature fetuses before

delivery, a zone of reduced density is usually seen around the fetal skull, produced by the subcutaneous fat layer. In 1947, Deuel described a separation of this transparent zone from the cranium by a layer of the same density as the other soft tissues of the fetus as a sign of intrauterine death.

The author presents his findings in the study of 64 dead fetuses, of which 40 had been examined before as well as after delivery. In more than 75 per cent of the cases examined before delivery a diagnosis of intrauterine death was possible. Deuel's halo sign was present in 9 cases.

Free gas appeared to be the most common and most important sign of fetal death. The gas usually forms in the vascular system. It is often demonstrable earlier than other signs of intrauterine death and may be the sole roentgenologic sign. The only factors which appear to have a positive bearing on the formation of gas are the degree of maceration and the maturity of the fetus. The more advanced both of these factors, the greater the formation of gas.

When fetal death occurs near term, free gas and Deuel's halo sign are frequently noted. When the fetus dies in an early stage of development, the most common roentgen evidence of death is the maceration of the trunk.

Three roentgenograms; 2 tables.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

THE GENITOURINARY SYSTEM

Clinical and Roentgenologic Considerations in Forty-Three Cases of Renal Tumors. Salvatore Galdini and Augusto Cirla. Radiol. med., Milan **44:** 643–662, July 1958. (In Italian) (Ospedale S. Anna, Como, Italy)

The authors assembled the records of 43 patients with histologically proved renal tumors. Thirty-four tumors were in males and 9 in females; 20 in the right and 23 in the left kidney. There were 4 cases in childhood (up to seven years of age), 1 in the fourth decade of life, 7 in the fifth decade, 13 in the sixth, 15 in the seventh, and 3 in the eighth decade. Histologically, 15 were "typical" and 9 "atypical" renal epitheliomata, 3 were classified as Wilms' tumor, 2 as papilloma of the kidney pelvis, 1 as a sarcoma, and 13 as hypernephroma.

Gross hematuria caused by neoplastic erosion somewhere within the pyelocalyceal walls was the presenting symptom in 36 cases. In the large majority of instances, a combination of plain (preliminary) abdominal roentgenography, excretory urography, retrograde examination, and retropneumoperitoneum appeared adequate for demonstration of intrinsic calyceal deformities and/or filling defects, or for extrinsic cystic pressure areas. The gas delineated the size of the tumor. Renal arteriography is sometimes helpful in showing vascular modifications, but it is of limited value and must not be regarded as part of the routine.

Most authors agree that diagnosis is likely to be made in the advanced stages of disease. This was true in 60 per cent of these 43 patients, 42 per cent of the total number dying within one year from the day of surgery. At that time 23 were still alive. At the time of publication, 11 patients were alive after nephrectomy. Five of these were between one and three years of age; 6 were between four and eleven years.

Twenty-six roentgenograms; 10 photographs; 1 table; 1 drawing.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Clinical Importance of Ureteral Duplication and Ectopia. Ian M. Thompson and Arjan D. Amar. J.A.M.A. **168:** 881–886, Oct. 18, 1958. (1405 East Ann St., Ann Arbor, Mich.)

Duplication of the urinary conduit system is the most common genitourinary anomaly. This occurs in 4 to 6 per cent of the population. With only about 0.5 per cent of these cases does ureteral ectopia occur. Yet of all the cases of this latter anomaly, more than 75 per cent are said to be associated with duplication. In the particular group of patients reported (number not stated), ureteral ectopia and duplication were found in association in 40 per cent.

Pathological processes which accompany or are associated with duplication and ectopia are due most frequently to the anomalous position of the lower ureteral orifice. Obstruction and infection are familiar features. Abnormality may occur in either portion of a duplication, but it is the upper segment, draining to a frequently malpositioned lower orifice, that is more prone to dysfunction.

Urography usually provides the first suggestion of the anomalous development. The abnormal upper kidney segment may not be opacified by intravenous urography. Radiographic findings include failure of an upper pole calyceal system to fill; downward and lateralward displacement of an otherwise normal collecting system; lack of an upper major calyx in what would otherwise be construed as a normal collecting system, indicative of the possibility of an unvisualized upper segment which ordinarily would be the upper calyx of a nonduplicated renal conduit. Less reliable is a lack of mirror image of the two kidneys.

Unexplained recurrent urinary infections with apparently normal pyelograms should suggest the possibility of unrecognized duplication and ectopic ureteral insertion. Careful search for ectopic orifices with bulb catheter injection, voiding cystourethrograms, retrograde urethrograms, and delayed intravenous urograms, is recommended. Ectopic ureteral insertion distal to sphincter control is not always associated with incontinence in the female.

Seven roentgenograms; 1 diagram.

B. JAY HILL, M.D.
University of Michigan

Comparative Study of Urographic Contrast Media. Loren E. Hart, Maurice D. Sachs, and Harry Grabstald. Arch. Surg. **77:** 75–78, July 1958. (H. G., 44 E. 68th St., New York 21, N. Y.)

A study of 4,136 patients with a variety of urographic media was done, and the results were graded as to diagnostic quality of the films and severity of patient reaction. It was found that nausea was the most commonly observed reaction, being most frequent with 30 per cent Urokon; this was decreased by addition of an antihistamine (Chlor-Trimeton).

The highest incidence of vomiting was with Urokon 50 per cent with diphenhydramine (Benadryl) in solution, but this was decreased when an additional 10 mg. of Benadryl was injected intravenously prior to the examination. Coughing, sneezing, flushing, and urticaria were most marked with Diodrast. Local reactions were high-

est with Neo-Iopax. There was only one case of shock, in this instance 50 per cent Urokon with 10 mg. of Benadryl was used. There were no deaths.

The overall reaction was highest with 35 per cent Diodrast and lowest with 50 per cent Urokon with 10 mg. Benadryl in solution, preceded by Benadryl intravenously, and with Neo-Iopax with 10 mg. of Chlor-Trimeton in solution.

The quality of the films varied. Neo-Iopax, which produced least nausea and vomiting, yielded the poorest pyelograms. The best films were produced by Miokon, Hypaque, Renografin, and 50 per cent Urokon. The authors state that further studies with the addition of antihistamines to the first three of these media should be undertaken. Reactions with 50 per cent Urokon were shown to be decreased by the addition of antihistamines.

One chart; 2 tables. GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

A Safe Contrast Medium for Urethrography. Ian M. Thompson. Am. J. Roentgenol. **80:** 627–630, October 1958. (University Hospital, Ann Arbor, Mich.)

Urethrography is most desirable in those conditions in which the vascular bed is exceedingly vulnerable and accessible. Disruption of continuity of the urethra by either disease or trauma will allow vascular ingress of any substance introduced into the urethra under pressure.

The author has found Thixokon a satisfactory medium in approximately 200 urethrographic studies in a variety of diseases. No untoward systemic or local effects were noted, irrespective of the type of pathologic process present in the urethra, prostate, or bladder. It was found to be an ideal medium for delineation of even minute fistulas and abnormalities in the newborn and was used without deleterious effects in severe and heavily infected strictures even with definite roentgenographic evidence of extravasation locally or into the vascular bed. It proved useful in defining a variety of obstructive conditions from vesical neck contractures in children to prostatic enlargements in the elderly. It is urged that all cases of hypospadias be subjected to urethrography to rule out occasional masked cases of intersex.

In view of the efficacy and safety of such media as Thixokon, the author believes urethrography should be more widely used.

Eight roentgenograms.

Thixokon Cystourethrography. James F. Glenn. Am. J. Roentgenol. **80:** 631–634, October 1958. (Duke University School of Medicine, Durham, N. C.)

The author has found Thixokon urethrocystography satisfactory in over 60 patients with a wide variety of pathologic conditions of the lower urinary tract. No instances of extravasation or untoward reactions occurred, although their possibility is always present as with other iodine compounds. Users of the medium are cautioned that it may deteriorate and its radiopacity be lost on exposure to daylight for prolonged periods.

The patient is centered over an 11 × 14-in. film. Approximately 15 to 20 c.c. of Thixokon is injected slowly into the urethra, with avoidance of undue pressure. The initial roentgenogram may be made during the terminal portion of the injection or it may be postponed until after the operator has left the room, since the thixotropic property allows retention of the agent in the urethra. If a subsequent oblique roentgenogram is desired, the patient is repositioned and an additional 15 to 20 c.c. of the medium is injected. Voiding urethrocystograms are also readily obtained. The factors are 25 mas (one-half second exposure at 50 ma) and 65 to 75 kv for the average patient.

It is suggested that Thixokon might be useful for fistulography elsewhere in the body.

Six roentgenograms.

THE SUPRARENALS

The Suprarenal Glands in Aortography. Sven Ahlbäck. Acta radiol. **50:** 341–350, October 1958. (Serafimerlasarettet, Stockholm, Sweden)

The vascular supply and contrast filling of the normal suprarenal gland were studied in a material consisting of approximately 100 lumbar aortograms obtained in patients without endocrinologic symptoms. In addition, 3 cases of adrenal tumors demonstrated by aortography are reported.

In the normal material, arterial supply was observed in only a few instances. Venous filling was demonstrated much more commonly. During the venous phase, the gland first presents a mottled appearance due to filling of large vessels; later, a diffuse homogeneous contrast filling of the parenchyma occurs. The right adrenal was contrast-filled in approximately one-half of the examinations. Normally it presents as a triangle, frequently with an indentation in its base, producing an "arrow-head" shape. As a rule, the normal right adrenal adjoins the upper renal pole, but in some instances a gap of 3 to 4 cm. exists between the latter and the base of the adrenal. The right posterior oblique position is best for demonstration of the right adrenal. The left adrenal is less frequently visualized, since it often lies in front of the kidney and is obscured by contrast material within the latter. Furthermore, the splenic vein often crosses the suprarenal region.

Aortography in two cases of cortical carcinoma revealed dilated arterial supply from the aorta and renal artery, irregular pathologic vessels within the mass, and diffuse contrast-filling of the tumor. In a third case, aortography demonstrated narrow arteries supplying a cortical adenoma in which diffuse contrast-filling occurred but no pathologic vessels were observed.

Rapid serial films are necessary during aortography carried out for demonstration of the adrenals, since contrast-filling of the latter occurs during a relatively brief period. If the adrenal is filled during aortography, the information obtained is more exact than in the case of retroperitoneal pneumography, since with the former method only the adrenal parenchyma is visualized.

Twelve roentgenograms.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

RETROPERITONEAL TUMORS

Primary Retroperitoneal Tumours. F. Duval. J. Fac. Radiologists **9:** 204–210, October 1958. (Peter MacCallum Clinic, Melbourne, Australia)

The author reviews the subject of primary retroperitoneal tumors based on a series of 39 cases proved by

biopsy or at postmortem examination. In a further group of 5 patients diagnosis was made by laparotomy or by pyelography.

In the main group of 39 cases the tumors occurred more frequently in males in the ratio 21 : 18. Although the greater number of cases were in the forty-to-seventy-year group, 30 per cent of the patients were under thirty years of age.

The majority of the tumors were malignant, and many arose from lymphoid tissue, 18 of the 39 cases falling into this group. Next most common were the tumors arising from connective tissue. The four undifferentiated neoplasms were considered by the pathologist to be primary tumors, not secondary, and in 2 cases postmortem examination had been carried out as well as biopsy.

In about two-thirds of the cases the first symptoms were abdominal pain, usually indefinite in onset and situation. Other common symptoms, often associated with pain, were diarrhea, loss of weight, and constipation.

A positive diagnosis of retroperitoneal tumor can be made on the following findings:

(1) The presence of an abdominal mass.

(2) Displacement of the ureters as seen in the pyelogram.

(3) Occasionally visualization of the tumor by a pneumogram.

The diagnostic points as shown by the retrograde pyelogram are summarized as follows:

(1) Anteroposterior films will show displacement of the ureter medially or laterally.

(2) Lateral films will show anterior displacement of the ureters.

(3) The calices may be distorted by pressure.

(4) The pelvis may be compressed or distorted.

(5) Muscle shadows may be obliterated.

(6) Displacement of the bladder may be noted.

In the present series, 21 patients of a total of 44 were treated by irradiation following laparotomy and biopsy; only 2 tumors failed to show response to irradiation. The majority of the tumors had their origin from lymphoid tissue, and they displayed the same sensitivity as tumors arising from lymphoid tissue in other parts of the body. Even when ascites and edema of the feet were marked and the patient's condition poor, palliation was often achieved and, in an occasional case, restoration to normal health over a period of years. On the basis of these figures it appears that deep x-ray therapy is the method of choice in the treatment of retroperitoneal tumors arising from lymphoid tissue.

The connective-tissue growths, fibrosarcoma, neurofibroma, and the single ganglioneuroma in this series responded poorly to irradiation, and irradiation of such tumors appears unlikely to prove of any value. Earlier diagnosis, while surgical removal is still possible, seems to offer the only hope in tumors of this nature.

No case of lipoma was treated by irradiation, but the single leiomyoma proved to be moderately radiosensitive, as shown by decrease in size and relief of symptoms. When the histology of the tumor is unknown, deep x-ray therapy should be tried, as in a large proportion of cases the tumor will be found to be radiosensitive. The best results in this series have been obtained in such cases.

Six tables.

THEODORE E. KEATS, M.D.
University of Missouri

TECHNIC

Apparatus for Remote Injection in Radiodiagnostic Procedures. D. J. Tibbs and W. G. Leslie. Lancet **1:** 1158–1159, May 31, 1958. (D. J. T., University of Durham, Newcastle-upon-Tyne, England)

An apparatus to protect the operator from undue irradiation during the injection of radiopaque media has been designed. A considerable length of tubing (No. 4 gauge—Portland Plastics) of a bore slightly greater than that of the needle connects the needle to the syringe. This tubing is light in weight, transparent, capable of resisting any pressure the syringe can deliver, and withstands repeated sterilization by heat. Special connectors are used to join needle and syringe to this tubing without any reduction in the effective lumen; flanging of the tube ends is not necessary. The nylon tubing passes through the connector and its rubber diaphragm; when the screw collar is firmly tightened the rubber is compressed and grips the tubing. A mechanical device, which in its essentials is a "window winder," is used to hold the syringe. Injection is conducted effortlessly with one hand almost at arm's length, with no tendency to drag on the tubing and no fear of the syringe breaking in one's hand. This apparatus is said to work at low pressure and impart an instant sense of resistance if the needle is not properly situated.

The apparatus, including the syringe pusher, has been found satisfactory for abdominal aortography and splenoportal venography. The same basic set, with the addition of appropriate needles and cannulae, has been used repeatedly for femoral arteriography, peroperative cholangiography, and presacral retroperitoneal insufflation of oxygen. For these procedures the syringe is, of course, operated by hand.

Three photographs.

Simultaneous Cholecystography and Urography with a New Medium "Duografin." Theodore L. Orloff. Am. J. Roentgenol. **80:** 618–619, October 1958. (8665 Clifton Way, Beverly Hills, Calif.)

A new radiopaque medium, Duografin, for simultaneous visualization of the biliary and renal systems, was employed in 25 cases. It contains in each cubic centimeter 400 mg. of Renografin acid, 200 mg. of Cholografin acid, and 198 mg. of methylglucamine.

The urinary tract was visualized satisfactorily in all cases; visualization of the common duct was good in 7 cases, fair in 17, and not obtainable in 1. There were no severe reactions, nor were warmth, venous pain, urticaria, nausea, or vomiting observed.

This medium is said to be indicated in abdominal diagnostic problems where the history suggests involvement of either the biliary or renal system and in routine physical examinations where time is a factor.

Two roentgenograms.

MISCELLANEOUS

Brucellosis and Echinococcus in Argentina. A Short Clinical and Radiological Report. H. H. Weber. Schweiz. med. Wchnschr. **88:** 567–570, June 7, 1958. (In German) (Hospital de Córdoba, Córdoba, Argentina)

The author reports on 5 cases of brucellosis and a case of echinococcosis which he observed in Argentina during a visit to Di Rienzo's clinic.

In Argentina, infection with *Brucella melitensis* is more common in women and children because of their contact with small animals such as sheep and goats. Infection with *Brucella abortus* Bang is more common in adult males, who care for cows, horses, and pigs. Brucellosis melitensis often affects the joint and bone system, and 75 per cent of the cases show characteristic clinical and radiological findings, although serologic and bacteriologic verification is always necessary.

The first radiologic signs are found at the vertebral contour. The bodies of the vertebrae, as well as the disks and ligaments, are affected. In the early stage the osseous structure shows loss of definition followed by bone destruction, swelling and, later on, narrowing of the disk. We find in cases of osteitis caused by brucellosis a distinct tendency to periosteal reaction and apposition of bone, such as are found in tuberculous infection. Fatal cases are due to purulent spinal meningitis. The lower dorsal and lumbar spine are often affected, the changes resembling spondylitis tuberculosa. Other common localizations are the pelvic joints, sacroiliac joints, and symphysis pubis. A pulmonary abscess caused by *Brucella* was found in one of the author's patients, a sixteen-year-old boy.

Echinococcosis is most common in the lung. Of 139 lung resections in 1957, 22 were done for that disease. Echinococcal nesting in the lung, as a hydatid cyst, is often an indication for surgical intervention, such as enucleation and lobectomy. The radiologic features vary according to the stage of evolution of the cyst or its complications and are characteristic and helpful to the surgeon. Bronchography and tomography are indispensable. The cyst causes spreading of the bronchi evident in the bronchogram. At times, air is noted between the pericyst and the membrane of the *Echinococcus* itself. This can be demonstrated in tomographs. Complicated echinococcosis has the appearance of a lung abscess. Sometimes, so-called floating-membrane remanents can be noted within the abscess cavity. These cause the *signo de camalote* of Argentine radiologists.

The cysts grow to the size of an orange and, as long as they are not infected, contain clear or yellowish fluid surrounded by a membrane (membrana adventitia or pericyst). This membrane is not formed by the *Echinococcus* itself, but is a reaction in the invaded organ and must be removed with the actual cyst.

Twelve roentgenograms.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

RADIOTHERAPY

Carcinoma of the Extrinsic Larynx. Frank C. Marchetta, Henry C. Riegler, and Walter T. Maxwell. Surg., Gynec. & Obst. **107:** 429–432, October 1958. (Roswell Park Memorial Institute, Buffalo, N. Y.)

A comparison of radiation and surgery in the treatment of carcinoma of the extrinsic larynx is made on the basis of experience with 304 consecutive patients at the Roswell Park Memorial Institute from 1935 to 1955. The extrinsic larynx is defined as that portion of the larynx above the free margins of the ventricular bands (false vocal cords). Thirty-four patients were excluded from the study because they did not return for biopsy or treatment, or, in a few cases, were treated without biopsy. All of the remaining 270 patients had positive biopsy reports of squamous-cell carcinoma.

In this series the age range was from thirty to eighty-six years, with a peak during the fifth and sixth decades. Ten per cent of the patients were females.

The most frequent symptom encountered was hoarseness. This was present in 74 per cent of the cases and in all patients with involvement of the vocal cords. Dyspnea occurred in 15 per cent and was noted especially with lesions involving the vocal cords. Sore throat was seen in 62 per cent and dysphagia in 58 per cent, being the most common complaints in patients with disease of the epiglottis, arytenoids, and aryepiglottic folds. Cough was present in 27 per cent, hemoptysis in 17 per cent, and a lump in the neck in 30 per cent.

In almost every case the carcinoma was visualized with a laryngeal mirror, although the extent was more accurately appraised by direct laryngoscopy at the time of biopsy. In most patients the primary lesion was well advanced and of considerable size (2 to 4 cm.) at the time of examination. Cervical nodes 1 cm. or greater in diameter were considered clinically significant. The authors noted an increase in metastases with involvement of structures higher in the larynx: in patients with lesions of the extrinsic cord metastases were present in 40 per cent; with epiglottic lesions, 62 per cent; with lesions of the aryepiglottic folds, 67 per cent. The incidence of positive nodes as determined surgically was 60 per cent.

A total of 241 patients received radiation therapy. This consisted almost exclusively in external irradiation, although prior to 1943 a few patients were given supplemental radiation with a radium pack or radium seed implantation. The external source was a 200-kv machine; 2 anterolateral portals were used, and the h.v.l. was 0.9 mm. Cu. A total tumor dose of 4,500 to 6,000 r was delivered in four to five weeks. Recently a few patients were treated with a 400-kv machine.

At the end of twenty-four months 78 per cent of the patients receiving radiotherapy were dead of their disease, 4.5 per cent were living with clinically detectable disease, 2.1 per cent were dead of other causes but free of cancer at the time of death, 1.3 per cent were dead of other causes but with active carcinoma at the time of death. Only 14.1 per cent showed no evidence of cancer at the end of the twenty-four month period.

Since 1953 surgery has been considered the treatment of choice. In 14 cases total laryngectomy alone was performed, but discovery of positive nodes in 60 per cent of surgical specimens has led to adoption of total laryngectomy with radical neck dissection as basic therapy for all patients with carcinoma of the extrinsic larynx. Results at the end of twenty-four months showed 27 per cent of the patients dead of their disease; 7 per cent were living with disease; 14 per cent died of other causes but presented no evidence of cancer at the time of death; 45 per cent were clinically free of cancer. The operative mortality was 7 per cent.

The authors believe this comparison indicates a definite improvement in survival for patients treated surgically. They hasten to add, however, that the

surgical cases were too few in number to warrant any positive statements.

Three photographs; 2 charts; 1 table.

ROBERT JACOBS, M.D.
University of Pennsylvania

Carcinoma of the Breast in Middletown, U.S.A. Thomas C. Moore, Donald R. Judd, and Will C. Moore. Surg., Gynec. & Obst. **107:** 433–441, October 1958. (Ball Memorial Hospital, Muncie, Ind.)

The authors report a sixteen-year unselected experience with carcinoma of the breast from a representative, middle-sized, essentially self-contained community, Muncie, Indiana. Postoperative follow-up was obtained in 100 per cent of the 307 consecutive cases of histologically verified carcinoma of the female breast seen at the Ball Memorial Hospital during the period between 1935 and 1951. All living patients have been followed for a minimum period of six years.

The Halsted type of radical mastectomy was carried out in 271 of 305 primary cases (89 per cent). Simple mastectomy was undertaken in 31 cases and biopsy only was performed in 3. Radical mastectomy was employed as the operation of choice, while simple mastectomy was reserved largely for the more elderly patients. Little effort was made to utilize any criteria of operability such as suggested by Haagensen and Stout.

The five-year survival of the total group of 307 patients was 54 per cent. The five-year survival of those 271 patients managed by radical mastectomy was 55 per cent and that of the smaller simple mastectomy group was 45 per cent. The authors analyzed the five-year survival by age groups and by age groups with and without axillary metastasis.

The most important single factor influencing the survival of the patient was found to be the presence or absence of axillary node metastasis. Axillary metastases were encountered in 52 per cent of the patients managed by radical mastectomy. The five-year survival in this group was 73 per cent without axillary metastases and only 31 per cent when axillary involvement was demonstrated.

Radiation therapy (1,800 to 2,000 r) was given following radical mastectomy in 57 patients. In the absence of axillary metastases this produced no improvement in five-year survivals. On the other hand, in the relatively small group of 36 patients with axillary nodes the five-year survival rate following postoperative irradiation was 53 per cent as compared with 34 per cent among 104 patients in whom this measure was not taken. The authors suggest that postoperative radiation might be used to greater advantage in doses higher than they have reported.

Ten-year follow-up was obtained in 100 per cent of a group of 184 consecutive patients. Of the total group, 33 per cent were alive ten years following operation. Radical mastectomy was performed in 164 of these patients with a 44 per cent ten-year survival in patients without axillary metastasis and a 22 per cent survival in patients with axillary involvement.

The authors stress the importance of ten-year survival statistics, since they appear to provide a more realistic picture of the success or failure in the management of carcinoma of the breast than may be obtained from the study of five-year survival results alone.

Six graphs; 9 tables.

DAVID E. KUHL, M.D.
University of Pennsylvania

Breast Cancer in Connecticut, 1935–1953. Study of 8,396 Proved Cases. Allan J. Ryan, Matthew H. Griswold, Edward P. Allen, Rolf Katzenstein, Richard Greenberg, John Keogh, and Charles Wilder. J.A.M.A. **167:** 298–307, May 17, 1958. (A. J. R., 147 W. Main St., Meriden, Conn.)

The authors present a study of breast cancer in Connecticut based on reports of 8,396 microscopically proved primary cases collected by the Connecticut Cancer Registry during a nineteen year period (1935–53). For purposes of comparison, the cases were divided into two seven-year groups and one five-year group, referred to as Groups I (1935–41), II (1942–48), and III (1949–53).

Comparison of Group I with Group II revealed an increase from 46.3 to 51.0 per cent in the number of patients surviving five years after diagnosis. This appears to be accounted for largely by improved survival of patients with evidence of regional metastasis. There was a consistent failure of about 30 per cent of the patients thought to have localized cancer to survive five years. In Group II, the five-year survival for patients with regional metastasis treated by radical surgery alone was 41.1 per cent and for those treated by radical surgery plus irradiation, 42.7 per cent. There is a significant difference favoring the survival of those patients treated by radical surgery over those treated by limited surgery in this study. The statement of the surgeon was accepted with regard to "radical" mastectomy. All other surgical procedures except biopsy were classified as "limited" surgery. There was no uniformity in the selection of patients for surgery with or without radiation therapy, in the choice of the type of surgery, or in either the surgical or radiological procedures.

The one group which showed a significant improvement in survival rate were those who received radiation after radical surgery. The improvement in the presence of regional metastasis was greatest in those patients aged fifty-four and under. Comparison of the number so treated who were free of their disease in five years with the number merely surviving indicates differences of 6 to 8 per cent. The authors believe that this improvement may represent actual control of the disease rather than simply a longer survival.

This experience suggests that more attention be given to administering postoperative radiation to patients having had radical mastectomy, regardless of a favorable prognosis. With radical surgery alone in localized disease there was 1.9 per cent improvement in survival in Group II over Group I, and in those with regional metastasis 2.5 per cent improvement. With radical surgery plus postoperative radiation there was improvement in survival for localized disease of 6.8 per cent and for regional metastasis of 8.6 per cent. Details of radiotherapy are not given except that most of the treatment was by 220-kv radiation.

The authors conclude that the combination of radical surgery and postoperative irradiation should be given every patient who satisfies the criteria of suitability for treatment. In this series, the woman who had a cancer in one breast was five times as likely to develop one in the other breast as a woman who was cancer free. The outlook for younger women was no worse in terms of survival than for older women, whether the disease was originally localized or involved regional nodes.

Sixteen tables.

NORMAN L. ARNETT, M.D.
Anaheim Calif.

Implant Radiation Therapy for Carcinoma of the Pancreas. Paul V. Harper and Katherine Lathrop. Arch. Surg. **77:** 613–620, October 1958. (University of Chicago, Chicago, Ill.)

The authors report their experience in the palliative treatment of 14 nonresectable carcinomas of the pancreas, using an implant of polyethylene tubing filled with a specially prepared concentrated solution of I^{131}, the use of which they have reported earlier (Surgery **40:** 270, 1956. Abst. in Radiology **68:** 787, 1957).

The implant is constructed by sewing the tubing around and through the tumor following as closely as possible the Paterson-Parker distribution rules. Both ends of the tubing are brought out through the skin and subsequently, when the patient has recovered from the surgical procedure, the tubing is filled with the isotope solution.

With the authors' technic approximately 10,000 to 15,000 r is the local tissue dose. Adjacent normal structures have not presented complications, but the method seems best suited for tumors somewhat removed from the head of the pancreas to avoid overirradiation of the duodenum. The maximum tumor size for successful treatment is 100 gm. The largest amount of activity which can be safely implanted is 150 mc. When the treatment has been completed, the ends of the tubing are sealed off and allowed to retract beneath the skin and the tubing is left in place permanently.

Pain relief is the primary goal of the procedure and in some cases palliation was gratifying. Advantages of the method are that all radiation hazard to the operator is eliminated; prior planning is not necessary, the only requirement being that sterile tubing be kept on hand. The isotope may be placed in the implant days or weeks after operation. If the patient should die with radioactivity within the body, it is easily removed and disposed of. The disadvantages are those of any form of implant therapy. The method is routinely accompanied by transient anemia and leukopenia if over 100 mc of isotope solution is administered.

Two roentgenograms.

MAJ. MARTIN A. THOMAS, M.C.
MacDill AFB, Tampa, Fla.

Surgical and Radiologic Treatment of Cancer of the Cervix in 397 Cases. Henry Clay Frick, II, James A. Corscaden, Harold W. Jacox, and Howard C. Taylor, Jr. Surg., Gynec. & Obst. **107:** 457–468, October 1958. (College of Physicians and Surgeons, Columbia University, New York, N. Y.)

The five-year end-results in 368 patients treated for cancer of the cervix during the years 1946–1951 are reported by the authors. These patients were admitted to either the Sloan Hospital for Women or the Francis Delafield Hospital (New York City). The International Classification with the amplification of subdivisions for Stage 1 and Stage 2 was employed. Treatment was by (1) intracavitary radium, (2) interstitial radium, and (3) radical hysterectomy.

Intracavitary radium was applied by the Curie technic. The relative cure rate for all patients in Stage 1 was 56.9 per cent. In Stage 2, the cure rate was 40.5 per cent. Two out of 12 patients survived five years in Stage 3 and none of 6 in Stage 4. The relative cure rate for all patients treated with intracavitary radium was 44 per cent.

One hundred and two patients were treated with interstitial radium. The only patient in Stage 1 died at five years. The five-year survival rate for patients in Stage 2 was 50 per cent and in Stage 3, 20 per cent.

External irradiation was the sole treatment in 22 cases, with 3 apparent five-year cures, 1 in Stage 4.

There were 87 cases treated by surgery and, in most of these, postoperative external irradiation was also given. The relative survival rate for Stage 1 was 86.5 and for Stage 2, 42.1. The authors note that of the 16 patients in stage 1A, the group in which the lesion was not clinically evident, 1 had parametrial extension and 3 had positive pelvic lymph nodes at the time of surgery.

The five-year cure rate for Stages 1 and 2, when surgery was the primary mode of therapy, was 86.5 and 42.1 per cent. The figures for those treated by intracavitary and interstitial radiation were 56 and 44.1 per cent.

The authors conclude that surgical treatment in Stage 1 cases yields a higher five-year survival rate than radiation therapy. They do state, however, that various factors, particularly case selection, make the two series not wholly comparable.

Two roentgenograms; 11 tables.

JOSEPH WINSTON, M.D.
University of Pennsylvania

Late Results of Radium Therapy in Cervical Carcinoma: A Clinical-Statistical Study on 798 Patients Treated at The Radium Centre, Copenhagen, During the Period 1922–1929. Bent Sørensen. Acta radiol. Suppl. 169, 1958. (Gentofte, Denmark)

A comprehensive clinical-statistical study of the late course of cervical carcinoma treated by radium is reported. The primary purpose was to determine whether patients with cervical carcinoma are permanently cured by radiotherapy. The series studied comprised 798 patients with a diagnosis of cervical carcinoma, who were seen during the period 1922–29 in the Radium Centre, Copenhagen. None of the patients in the series had received curative therapy elsewhere. Cases referred for prophylactic radiotherapy following hysterectomy or for treatment of recurrences were excluded from the study. All other patients with cervical carcinoma, including 6 who were not treated because they were seen in a terminal state, were included. The minimum follow-up period was twenty-five years.

The treatment method was a modified Stockholm technic of pure radium therapy, with two applications separated by an interval of ten days. At each administration, the intracavitary dose of radium was 60 to 70 mg. and the vaginal dose (against the cervix) 100 mg. The duration of each application was twenty hours. The total dose for complete treatment was 6,400 to 6,800 mg. hours. No patient had primary operation and roentgen irradiation was not given routinely. In 1922, 17 of the patients received a divergent method of treatment, with an average dose of about 10,000 mg. hours.

The necessary information for follow-up was obtained by the use of hospital and out-patient department records, government vital statistics, reports of burial authorities, and files of health insurance societies. Of the 798 patients in the series, only 6 could not be traced. The cause of death of 20 patients was

indeterminate, but in all the rest it was felt that this could be accurately ascertained for the purposes of the study. Of the 798 patients, 59 were still alive at the time of the follow-up and all of these were interviewed. One patient was found to have a recurrence of disease.

The gross results of the study are as follow:

59 or 7.4 per cent were alive
614 or 76.9 per cent had died of cervical carcinoma
20 or 2.5 per cent had died of uncertain cause
14 or 1.8 per cent died of a second cancer
84 or 10.5 per cent died of intercurrent disease
1 patient represents a primary diagnostic error, that is, she did not have cervical carcinoma
6 or 0.8 per cent were untraceable

When the duration between treatment and death (regardless of cause) was calculated, it was found that survival time was considerably shortened in comparison to a "normal" population. Analysis of the case histories revealed that recurrences accounted for the decrease in survival time.

The study demonstrated that the primary spread or stage of disease correlated well with the number of five-year survivors. Among the ten-year survivors, however, the probability of recurrence did not correlate with the primary spread or stage of disease. The incidence of late recurrences decreased as time passed.

Only a slightly greater number of patients died of intercurrent disease than would be expected if they died as indicated in Danish vital statistics. This is of interest, since these patients had received large doses of ionizing radiation to the pelvis. Furthermore, the number of multiple cancer in the series was not larger than might be expected on a statistical basis.

Of the patients who died of intercurrent disease, 6 had late therapeutic complications of radium therapy, which may have been a contributory cause of death. Most of the therapeutic complications were ureteral strictures.

The conclusion of the study is that "there are indeed patients who are permanently cured of cervical carcinoma, that their primary disease and its treatment do not predispose to the development of multiple cancers, and that the prognosis in the cured cases is only negligibly deteriorated by the treatment." Over 25 per cent of the deaths occurring after the fifth year and about 10 per cent of the deaths occurring after the tenth year were due to late recurrences. In about 6 per cent of the patients late therapeutic complications developed. It is advisable that all patients treated for this condition be followed until they die.

Twenty-eight photomicrographs; 16 graphs; 41 tables.

ERNEST R. DUVALL, M.D.
The Henry Ford Hospital

The Radiation Reaction in the Vaginal Smear and Its Prognostic Significance: Studies on Radiologically Treated Cases of Cancer of the Uterine Cervix. Olle Kjellgren. Acta radiol. Suppl. 168. (Konung Gustaf V:S Jubileumsklinik, University of Gothenburg, Sweden)

The author gives a thorough review of the literature on the effect of radiation on vaginal smears, and describes his own cytological technic. He studied two series of patients, both of which received combined radium and roentgen irradiation, according to the Stockholm technic. Series 1 consisted of 241 patients seen during a certain time interval on whom smears were taken prior to the second or third radium applications. Series 2 was composed of 46 ambulant patients living in the same town as the clinic, on whom smears were taken three times per week.

The measure of radiation response was the percentage of benign exfoliated epithelial cells which showed radiation changes. The response was considered good when 60 per cent or more of the benign exfoliated cells met any of the following criteria:

1. *Size increase:* major axis measuring more than 35 microns for basal cells or 68 microns for intermediate and superficial cells.
2. *Nuclear changes:* multinucleation, deformity, and wrinkling or karyorrhexis or, in a basal cell, karyopyknosis.
3. *Cytoplasmic changes:* vacuolization or "fibril" formation; bizarre shapes; in the case of basal cells modified staining properties.

The criteria for size increase was based on a study of a large number of normal cells.

In Series 1, the author found a 36.5 per cent five-year cure rate in the group with poor radiation response as determined by the vaginal smear, and a 73.9 per cent five-year cure in the cases with good response. It appeared that the radiation reaction was essentially independent of the staging of the tumor, the duration of the history, the number of pregnancies, gross appearance, or the radium dosage within therapeutic limits. Younger patients, however, showed a poorer response frequency. The rate of primary local healing (no evidence of tumor on clinical examination of the cervix or upper vagina) was even more significantly related to the cytological response. The local five-year healing rate in all stages was 91.3 per cent in the good response group and 50.8 per cent in the poor response group Again, this difference was present in all stages, the best correlation being present in Stage II. Another interesting finding was that, among the patients who died during the observation period of five years, those in the good response group tended to survive longer than those in the poor response group. The frequency of vesical and rectal injury, however, was three times as great in the good response group as in the poor. This is apparently not fully significant from a statistical point of view.

Series 2 was used to study the changes in radiation response with respect to time. It was found that the maximum changes were apparent about the twelfth day after the first treatment and ten and a half days after subsequent treatments. The radiation reaction in the vaginal smears taken at the time of the first and second radium insertions was representative of the actual radiation reaction in most cases, although 14 per cent of patients whose serial smear showed a good response did not show a frequency equal or exceeding 60 per cent of the time of subsequent radium treatment, so that in Series 1 some good response cases were probably missed.

The results of the author's investigation agree with those of Ruth Graham (see, for example, Cancer **8:** 59 and 71, 1955. Abst. in Radiology **66:** 153 and 154, 1956) who showed a somewhat higher correlation. However, the groups are not entirely comparable, as the present study was based largely on the response to the first and second radium applications as observed at the time of subsequent application, and some good re-

sponses may no longer have been apparent by the time the next smear was taken.

The author concludes that the radiation reaction seems to be an inherent response to the irradiation of the host tissue, and that "the cytological response is correlated with the prognosis in the sense that a good response is associated with a higher local healing rate, and hence, with a higher five-year apparent recovery rate. It seems to be uncorrelated with the incidence of metastatic spread. If a good cytological response fails to materialize under ordinarily favorable conditions, the prognosis will be poor. If a good cytological response is obtained in otherwise unfavorable circumstances, the prognosis will be good."

One color plate; 72 charts; 32 tables.

ANDREW POZNANSKI, M.D.
The Henry Ford Hospital

Lymphosarcoma in Childhood. Saul A. Rosenberg, Henry D. Diamond, Harold W. Dargeon, and Lloyd F. Craver. New England J. Med. **259:** 505–512, Sept. 11, 1958. (Memorial Center for Cancer and Allied Diseases, New York, N. Y.)

Twelve hundred and sixty-nine cases of lymphosarcoma were seen at Memorial Center for Cancer and Allied Diseases between Jan. 1, 1928, and Jan. 1, 1958. Of this group, 69 patients (5.4 per cent) were fifteen years of age or below. These constitute the basis for this report.

The general term lymphosarcoma includes 3 subgroups: giant-follicle lymphosarcoma; (2) reticulum-cell sarcoma, in which group the predominant cell type is greater than one and a half times the size of the mature lymphocyte; (3) lymphosarcoma, in which the predominant cell type is similar to the mature lymphocyte. The distribution of these types among the 69 children was as follows: giant-follicular lymphosarcoma, 2.9 per cent, reticulum-cell sarcoma, 36.2 per cent, lymphosarcoma, 60.9 per cent. Males predominated in the series, 2.6 to 1; in late childhood (eleven to fifteen years of age) the preponderance was 4.5 to 1. Peripheral lymph node enlargement was an initial symptom in 43.1 per cent as compared to 65.4 per cent in adults. An intra-abdominal tumor was more common in children, 23.1 per cent as compared to 11 8 per cent in the older group. Bone lesions were much commoner in children, 13.8 per cent as compared to 2.4 per cent in adults.

Roentgenographic manifestations of lymphosarcoma in children parallel those seen in adults. In 60 children who had x-ray examination of the chest, 31 (51.7 per cent) had evidence of intrathoracic lymphosarcoma. Mediastinal hilar adenopathy was seen in 35 per cent, pleural effusions in 30 per cent, and pulmonary parenchymal lesions in 15 per cent. Bone lesions before therapy were osteolytic in the great majority of cases.

Anemia and thrombocytopenia prior to therapy were not a problem. Subsequently anemia developed in over half the children, usually after chemotherapeutic agents had been used. Radiation therapy in this group resulted in only an occasional transient leukopenia. Of the total group, 10 (14.5 per cent) showed a transition suggesting a leukemic change. In 7 of the children primary reticulum-cell sarcoma appears to have occurred in bone. In such instances, the tumor is radiosensitive and metastasizes late, thus demanding aggressive extirpative therapy. Three of the 10 surviving children were from this group.

The judicious use of x-ray therapy continues to be the backbone of the therapeutic program. It provides relief of distressing symptoms and may be life-saving, if only for an unpredictable period. The use of polyfunctional alkylating agents alone, combined with adrenal steroids, provides little, if any, lasting benefit to the majority of children. The antimetabolic drugs, chiefly the folic acid antagonists, appear to have a wider field of usefulness, largely in children with acute leukemia. In specific problems, such as superior vena cava obstruction and spinal cord compression, the polyfunctional alkylating agents administered before radiation therapy appear to be useful for both their anticongestant and their antitumor effects. Supportive therapy utilizing blood transfusions, antibiotics for specific infections, parenteral infusion of fluids, and surgical correction of obstruction of the intestine or upper trachea, can be temporarily life-saving.

Occasionally the disease is in an apparently localized unicentric site, and efforts at total eradication by surgical and/or radiologic means are justified. In selected cases, repeated attempts to destroy recurrent disease are justified and occasionally rewarding.

The not infrequent long-term survival (8 cases in the authors' series) justifies some optimism and should discourage the defeatist attitude that is too often seen.

Four figures; 3 tables.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Roentgen Tube with Bifocal Rotating Cathode for the Production of Convergent Beams. Mario Lenzi, Carlo Brameri, and Franco Baracchi. Radiol. med. Milan **44:** 663–670, July 1958. (In Italian) (Instituto di Radiologia dell' Università di Modena, Italy)

The senior author has experimented, since 1936, with various procedures intended to provide a more efficient concentration (convergence) of the roentgen beam. His latest (1957) achievement is a custom-built roentgen tube with a cathode made of 2 coaxial filaments which rotate as a core, surrounded by a circular tungsten anode. The resultant, conically shaped beam of roentgen rays exhibits a maximum of radiation intensity not at the exit from the tube, but at the "epicenter" of the cone. The "depth" of this maximum depends on the construction of the anode as well as on the energy utilized. In a tested model, when air doses were computed, the maximum was at about 18 cm. from the tube wall, as shown in a diagram and in a roentgenogram of the beam in air. Another roentgenogram, of the beam in a paraffin phantom, suggests that a similar conical distribution will probably be obtained in patients. The therapeutic possibilities of such a method are self-evident, but so far the procedure is still in the experimental stage.

Two roentgenograms; 2 photographs; 2 drawings; 1 graph.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Spectral Distributions of 280 kVp X Rays. D. V. Cormack, W. E. Davitt, D. G. Burke, and E. G. Rawson. Brit. J. Radiol. **31:** 565–570, October 1958. (University of Saskatchewan, Saskatoon, Sask., Canada)

Primary and scattered spectra of 400-kvp x-rays were presented in an earlier paper (Brit. J Radiol. **30:** 129, 1957. Abst. in Radiology **70:** 146, 1958). The scintillation spectrometer measurements are now extended to three qualities of 280-kvp radiation.

Some inconsistencies were found between attenuation factors calculated from earlier measurements and those obtained by direct measurement. It was therefore decided to remeasure. It is felt that the earlier error resulted from distortion of the spectrum by the thick wall of the crystal.

Tables give the spectral distribution for primary radiation of h.v.l.'s 1.8, 2.6, and 3.1 mm. Cu, for a field 300 cm.², and for h.v.l. 2.6 mm. Cu for a field of 50 cm². In each case the spectra were measured at depths of 0, 2, 5, and 15 cm. The ratio of energy absorption in bone to that in muscle is given for each depth.

The measurements were checked by calculating h.v.l.'s for the primary radiation and checking these against experiment; also by comparing the calculated attenuation in water against the "zero area" values of Johns.

Six figures; 6 tables.

LUCILLE DU SAULT
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RADIOISOTOPES

The Use of Radioactive Phosphorus for the Detection of Intraocular Tumours. R. C. Tudway and A. Palin. Brit. J. Radiol. **31:** 549–555, October 1958. (Bristol Royal Hospita', Bristol, England)

The preferential uptake of P^{32} in tumor cell nuclei, demonstrated by other investigators, suggested a means of tumor detection with a Geiger counter. The eye was chosen for investigation for two reasons. First, many eyes have been needlessly sacrificed owing to a diagnosis of probable malignant tumor; econd, because of the possibility of choosing counting points for which equivalent controls were available.

Because of radiation hazard, young persons were accepted for the test only if the results would be a significant factor in treatment. Dosage in older persons was 700 μc/70 kg. body weight and in young persons, about half that.

Intravenous injection and immediate counts were done early in the series, as well as counts at twenty-four or forty-eight hours. Although the counting rates are highest twenty to sixty minutes after injection, and differences between tumor and normal tissue are greatest (Krohmer *et al.*), they vary rapidly, so that it is difficult to obtain accurate comparative readings in such a short time. The oral route and twenty-four or forty-eight hour testing were finally adopted. The counts under these conditions are lower but are more consistent.

An end-window counter was used covered with a smooth Portex plastic skin. The counter is pointed to the center of the eye. An equal pressure is used for all counts. The patient looks in the appropriate direction for the meridian concerned. A local anesthetic is employed.

Counts are made at 1, 3, 5, 7, 9, and 11 o'clock of both eyes, as far back as possible all around the eye. They are plotted on a visual field chart on the corresponding meridians. Extra readings as far back as possible on the lateral side may then be made to find a posterior tumor, or an extra meridian may be measured at a point of expected activity. The final result can be plotted as the "meridional differential" of the two eyes, and a line drawn at the 40 per cent excess difference level.

On the basis of 17 cases, 40 per cent excess uptake is recommended as strongly supporting malignancy in intraocular tumors. For posterior tumors just within the reach of the counter, 30 per cent or even a little less is recommended, provided the readings are consistent and repeated several times. For a posterior tumor the excess is less than for an anterior tumor. Active uveitis is the only other condition giving high readings but it is easily diagnosed clinically.

Consistent positive results were obtained in primary malignant melanoma and secondary carcinoma. There was no success in detecting retinoblastoma.

At present the test is not a substitute for clinical judgment but may tip the balance when other evidence is divided. Technic must be improved. Greater experience of the reliability of the test will encourage its greater use.

Fifteen figures; 1 table.

EUGENE A. CORNELIUS, M.D.
Houston, Texas

Screw-Implantation of the Pituitary with Yttrium-90. A. P. M. Forrest, D. W. Blair, and J. M. Valentine. Lancet **2:** 192–193, July 26, 1958. (Western Infirmary, Glasgow, Scotland)

Complete necrosis of the pituitary can be achieved by implanting two-6 mc rods of yttrium 90 into the sella turcica through twin cannulas inserted transnasally (one through either nostril) under radiologic control, and this method of treatment may benefit patients with advanced mammary cancer. Consistent and trouble-free destruction of the gland depends primarily on placing the two sources of radiation so that one lies in the center of each half of the gland. This was not always achieved in the authors' earlier method of implantation, and in a number of patients a troublesome rhinorrhea developed, presumably due to radiation necrosis of the diaphragma sellae because of faulty placement of the rods.

To overcome this difficulty a modified technic has been developed, for use with an image amplifier. In this procedure the holes in the anterior wall of the sella, through which the rods have been inserted, are plugged, providing an added protection against leakage of cerebrospinal fluid. The activated yttrium unit is fitted into one end of a stainless steel self-tapping orthopedic screw (Sherman screw size 6, 5/32 in. diameter) 0.5 in. long.

Fourteen patients with metastatic mammary cancer, considered unfit for adrenalectomy, have been treated by introducing twin screws each loaded with 5 to 7 mc yttrium-90 into the pituitary. Three patients died within three days from progression of the cancer, and in all 3 the gland was entirely destroyed except for a single layer of subcapsular cells. In 1 patient who died six weeks after implantation the pituitary was completely destroyed.

The authors previously described the use of radon for the destruction of the pituitary (Lancet **1:** 1054, 1955; **1:** 399, 1956. Abst. in Radiology **66:** 477, 1956; **68:** 462, 1957).

Six roentgenograms; 1 drawing.

Hypophysectomy Combined with Intrasellar Irradiation with Yttrium-90. Preliminary Communication. G. A. Edelstyn, C. A. Gleadhill, A. R. Lyons, H. W. Rodgers, A. R. Taylor, and R. B. Welbourn. Lancet 1: 462–463, March 1, 1958. (G. A. E., Royal Victoria Hospital, Belfast, Ireland)

A method is described for attempting to destroy the pituitary gland completely by surgical hypophysectomy followed by intrasellar irradiation with yttrium 90 in wax. Of 25 patients with advanced mammary carcinoma so treated, 20 survived operation and 16 were greatly improved.

One table.

Palladium^{103}: A New Isotope for Interstitial Implantation at Operation. Paul V. Harper, Katherine A. Lathrop, Louis Baldwin, Yoshio Oda, and Lidia Kryshtal. Ann. Surg. **148:** 606–614, October 1958. (University of Chicago, Chicago, Ill.)

Palladium 103 has a half-life of seventeen days and decays entirely by electron capture. A number of weak gamma rays are emitted but these are negligible from the point of view of radiation dosage. The only radiations of significance are the 20-kv characteristic radiation of the daughter isotope rhodium and the 37-kv conversion electron whose range in tissue is approximately 30 micra. The 20-kv rays have a half-value depth in tissue of approximately 1.0 cm. Physical and chemical properties of palladium are discussed, and methods and problems of producing the isotope are reviewed in moderate detail. For purposes of this study, the isotope is precipitated as palladium black and injected into tissues as a suspension. In rats there was very little migration of the isotope from the site of injection. Histologic studies show well localized radiation reactions. *In vitro* radiation patterns of the isotope obtained by photographic methods are presented.

It is theorized that palladium 103 may find a use in treatment of selected tumors by interstitial implantation. Advantages for the isotope include relative ease of handling, with ready shielding from the low energy gamma rays. This isotope also appears to present a relatively uniform radiation field of a more favorable pattern than other isotopes, including gold 198.

Three roentgenograms; 12 radioautographs; 6 photomicrographs; 1 graph.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Splenectomy in Hemolytic Anemia: Results Predicted by Body Scanning After Injection of Cr^{51}-Tagged Red Cells. Paul R. McCurdy and Charles E. Rath. With the technical assistance of Kenneth McCoy. New England J. Med. **259:** 459–463, Sept. 4, 1958. (Georgetown University School of Medicine, Washington, D. C.)

Fifty patients with various hematologic disorders were studied with body-surface scanning after the injection of red cells tagged with radioactive chromium. A maximum splenic-precordium ratio of radioactivity of 1.5 or more and a splenic localization index of 1.0 or more were found to correlate well with other information regarding increased hemolysis and with the results of splenectomy in 10 patients with hemolytic anemia.

The splenic localization index was found helpful in the interpretation of data by virtue of permitting mathematical expression of the importance of rate as well as magnitude in the changes of the splenic-precordium ratio. The time required for equilibrium of radioactivity over the spleen was found to be not uniformly reliable as an indication of the splenic sequestration and destruction of red cells. The "test" described by the authors, based on the maximum splenic-precordium ratio, the spleen localization index, and the clinical picture, appears to be a reliable method for selecting patients with hemolytic anemia for splenectomy.

Two tables and 8 case histories are included.

WYNTON H. CARROLL, M.D.
Shreveport, La.

Rotation Therapy with a Cobalt^{60} Unit. III. Integration of the Transmitted Beam as a Means of Estimating Tumour Dose. M. A. Bullen and W. R. Inch. Acta radiol. **50:** 395–409, October 1958. (Bristol Royal Hospital, Bristol, England)

The authors have done extensive experimental work and calculations to determine the feasibility of a calculated transmitted dose rate with rotational therapy using a Co^{60} source during one or more complete revolutions. For a cylindrical homogeneous phantom the results of this type of integrated transit measurement will be the same as those obtained by instantaneous rate readings at 10° rotation intervals. For noncylindrical outlines it is less simple to establish this identity. An experimental comparison of 9 patients undergoing rotation therapy, however, showed close agreement in resulting tumour-air ratios and an approximation to the calculated values based on the patient's physical outline (Johns' method).

Experimental relations between transit-ratio and tumor-air ratio for homogeneous phantoms of water, petrol, and ethyl alcohol are given and are in good agreement with calculated data.

This technic of computing the average tumor-air ratio is valid only when the tumor is fairly central in the field.

The possibility of tumor-dose controlled rotation therapy through integrated transit measurements with the use of a Victoreen Model 510 dosimeter is extensively discussed.

Nine diagrams; 2 tables. SAUL SCHEFF, M.D.
Boston, Mass.

Hematologic Findings in Human Beings Given Therapeutic Doses of Gallium-72. W. Wolins and V. P. Bond. Blood **13:** 865–873, September 1958. (Brookhaven National Laboratory, Upton, L. I., N. Y.)

The hematologic effects of gallium 72 administered intravenously to patients with diffuse bony metastases or primary bone cancer were studied. The effects of this internally administered isotope were, in general, similar to those resulting from total-body external radiation. The degree of effect was greater than that anticipated from estimates of the total-body dose received from the isotope. Localization in the bone may have been responsible for this finding.

The depth and duration of platelet count depression probably represented the best indices of the degree of marrow damage after radiation, and may be indicative also of the total damage sustained by the marrow from previous exposure.

The effects of large doses of radiation on the marrow appeared to be cumulative to a point of no return, beyond which regeneration may not be possible.

It was found that a total white count below 1,000 and a platelet count below 25,000 could be tolerated for weeks without infection or gross bleeding and with ultimate recovery. Therapy directed to these reactions did not appear to be indicated.

Twenty-one patients were treated. Four illustrative cases are presented.

Four figures.

WYNTON H. CARROLL, M.D.
Shreveport, La.

Thyroid Function and the Metabolism of Iodine in Patients with Subacute Thyroiditis. Sidney H. Ingbar and Norbert Freinkel. Arch. Int. Med. **101:** 339–346, February 1958. (Thorndike Memorial Laboratory, Boston City Hospital, Boston 18, Mass.)

Studies of thyroid function and the metabolism of iodine were performed before and after treatment in 10 patients with subacute thyroiditis. Eight of the patients were women and 2 were men. One was seventy-six years old. The ages of the other 9 ranged between thirty-four and forty-five years. Duration of symptoms at the time of the initial study was between two weeks and four months, averaging eight weeks. The erythrocyte sedimentation rate was elevated in all the patients, averaging 35 mm. in one hour. Distinct increases in the basal metabolic rate (BMR) were noted in 3 patients; decreases occurred in 7 patients following treatment, but only one value was outside the normal range. In the 7 patients in whom the measurements were made, values of the serum precipitable stable iodine (PBI^{127}) prior to therapy ranged broadly between 2.7 μg and 16.2 μg per 100 ml. Following treatment, normal values for PBI^{127} were found in all patients. Twenty-four-hour thyroidal uptakes of I^{131} were negligible or markedly diminished in all patients prior to treatment. Values averaged 3 per cent, and no value exceeded 8 per cent of the administered dose. Following therapy, values for thyroid uptake of I^{131} were normal in all but one case. In all patients prior to treatment, two distinct abnormalities were obtained in values for the butanol-extractable I^{131} (BEI^{131}): (1) In all patients with active subacute thyroiditis, values of BEI^{131} were greater at twenty-four than at seventy-two hours. This is in marked contradistinction to observations in normal or hyperthyroid patients or patients with thyroidal hypofunction. (2) Absolute values of BEI^{131} in all patients were well within the normal or hyperfunctioning range, despite the marked reduction in thyroidal accumulation of radioiodine. This complex of findings is best explained by the thyroidal synthesis of small amounts of iodinated materials which are then rapidly released from the gland.

Eight of the 10 patients were treated by external x-irradiation of the thyroid area (between 500 and 850 r, measured in air). One patient received cortisone intramuscularly and another thyroid-stimulating hormone (10 units daily for three days). These therapeutic regimens were followed by remission of symptoms. Concentrations of BEI^{131} were entirely normal in 6 of 8 patients following x-irradiation, and in all the patients receiving irradiation, the normal quantitative relationship between twenty-four and seventy-two-hour values were found.

From an analysis of the results, a hypothesis concerning the nature of the functional abnormality in subacute thyroiditis is formulated. It is suggested that two principal abnormalities in thyroid function occur. The first is a diminution, though not complete cessation, of hormonal biosynthesis. The second is a loss of the storage function of the gland, with passage into the circulation of a variety of iodinated materials. These functional abnormalities have been shown to be promptly restored to normal following x-ray therapy.

Improved Method of Labelling Red Cells with Radioactive Phosphorus. P. L. Mollison, Margaret A. Robinson, and Denise A. Hunter. Lancet **1:** 766–769, April 12, 1958. (Medical Research Council's Blood Transfusion Research Unit, Postgraduate Medical School of London, London, England)

When radioactive phosphorus is added to heparinized blood and the mixture is then incubated at 37° C., about 30 per cent of the P^{32} is incorporated in the red cells during the first hour. In the course of experiments on red-cell metabolism, the authors found by chance that the uptake of P^{32} by red cells washed in citrate was very much more rapid than this. Further investigation confirmed the finding that, when cells are washed once in citrate and are then incubated, phosphorus is taken up very rapidly, the process having a half-time of about five minutes. This acceleration over the rate normally obtained seems to be due to the removal of competing anions, since it is also produced when the red cells are washed in sucrose.

Red cells labeled in this way may conveniently be used for estimating the red-cell volume, because the rate of loss of P^{32} from such labeled cells is not significantly more rapid, either *in vitro* or *in vivo*, than that observed when they are labeled in the usual way.

The authors found the method not only more rapid but more complete than that currently employed. Hence the red cells need less washing. Very close agreement with simultaneous estimates made by the Cr^{51} method was obtained in 7 cases.

One graph; 4 tables.

The Relative Hazards of Strontium 90 and Radium 226. Margaret Hindmarsh, Maureen Owen, Janet Vaughan, L. F. Lamerton, and F. W. Spiers. Brit. J. Radiol. **31:** 518–533, October 1958. (M. H., Nuffield Department of Medicine, Oxford, England)

Using data from certain animal experiments, the authors have calculated the present maximum permissible body burden for Sr^{90} by comparison with radium, on the basis of clinical experience with luminous dial painters and persons given radium therapeutically. The errors involved are discussed. These include the extrapolation of data from small animals to man for effects where so little is known about the fundamental processes involved, the use of a single administration of the isotope for comparison with chronic exposure, and the use of high tumor incidence as a basis for conclusions about low incidence, there being some evidence that the latter is not parallel to the former.

A comparison of the maximum permissible burdens for strontium and radium on the basis of radiation dose presents many difficulties. The maximum range of the alpha particles of radium in bone is less than the shortest linear dimensions of the radioactive deposits observed in a man with a body burden of 0.48 μc (β and γ are ignored since their dose contribution is

not more than a few per cent of that of the alpha particles). In the case of Sr^{90}, the maximum range of the beta particles is about 6 mm. in bone and about 1 cm. in tissue. There is doubt about the correction factor which should be used for RBE of alpha particles.

It is suggested that the maximum permissible burden for Sr^{90} should be determined on a dosimetric basis without reference to radium.

Nine figures; 5 tables.

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RADIATION EFFECTS

Ocular Effects of Radiation. David G. Cogan. New England J. Med. **259:** 517–520, Sept. 11, 1958. (Harvard Medical School, Boston, Mass.)

A synopsis of ocular effects from ionizing radiations and other portions of the electromagnetic spectrum is presented. The corneoconjunctival epithelium, unlike the skin, has no protective covering of keratin and is only a few cells thick. Thus, some rays, as ultraviolet rays from a welder's arc, may cause a keratitis, though elsewhere they might produce only a mild erythema. The lens is especially vulnerable because it is avascular and has no cooling system. Its constituent cells are enclosed in a capsule which permits no exchange of cells with the rest of the body and no removal of debris. It is thus uniquely limited in its reparative processes by the fact that there is no migration of cells into and out of the lens.

Ionizing radiations of most practical concern are x-rays, gamma rays, beta particles, and neutrons. The relatively soft x-rays, 75 kv or less, will be absorbed superficially and cause simply a keratoconjunctivitis. Beta particles will generally have the same effect. On the other hand, the harder x-rays, gamma rays, and neutrons penetrate the eye more effectively and may cause, in addition to keratoconjunctivitis, cataracts and occasionally retinal damage.

In its mildest form the keratoconjunctivitis manifests a stippling of the corneal surface from loss of the superficial cells. In more severe forms it may present either as an indolent ulcer or a diffuse epidermalization of the cornea, depending upon whether the radiation has been applied locally to the cornea or widely to the entire eye and lacrimal apparatus. The dose necessary to cause these severe corneal complications is however so high (in the order of 2,000 to 3,000 r), that it rarely has much clinical significance.

Cataracts: Damage to the lens causes cataracts and these may result from amounts of radiation that do not cause clinical disturbances in other parts of the body. A radiation cataract is characterized initially by a dot at the posterior pole of the lens, and is best seen as a silhouette when viewed with the ophthalmoscope. This dot increases in size to form a disk-shaped plaque and then progresses to a granular opacification of the posterior subcapsular region, with eventual opacification of the entire lens. Contrary to popular belief, radiation does not hasten or in any way influence the development of other types of cataract.

There is a long latent period between the time of exposure and the onset of the cataract. The interval varies inversely with the dose. With heavier radiation it may be a matter of months, but with near threshold doses, it may be five years or more. The threshold dose for cataracts in human beings is in the order of 600 r (200 kv) or its equivalent. With this dose, the cataracts may not progress beyond the stage of posterior polar opacities. Cataracts from irradiation in excess of 1,000 r are usually progressive. The threshold dose for neutron cataracts appears to be less by a factor of 10.

Cataracts have developed in some of the earlier cyclotron workers exposed to an unknown amount of gamma and neutron radiation to the head region. Radiation cataracts have occurred in approximately 10 per cent of those who were within one kilometer of the hypocenter at Hiroshima.

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Visual Field Changes Produced by X-Ray Treatment of Pituitary Tumours. Max Chamlin. Brit. J. Ophth. **42:** 193–211, April 1958. (Montefiore Hospital, New York, N. Y.)

During the past ten years the author has examined ophthalmologically at least 180 patients with pituitary tumor (150 chromophobe adenomata, 30 eosinophilic adenomata) treated by x-rays. Most of the patients received an average total tumor dose of 3,000 r, usually divided into three courses of approximately 1,000 r, each course lasting from four to six weeks, with an interval of three to four weeks between courses. In a few instances treatment was given in a single course and completed in six to eight weeks; in a few it extended over a period as long as six to eight months.

In an investigation of the effect of x-ray therapy on the visual fields, the following cases were excluded: (1) those treated primarily by surgery but in which irradiation was given immediately postoperatively; (2) those in which adequate follow-up visual field studies could not be obtained; (3) those seen in consultation on only one or two occasions, either for diagnostic purposes or as a guide to therapy; (4) those with clinical evidence of pituitary tumor but without involvement of the visual fields. This selectivity left only 40 cases suitable for study.

Of the 40 cases, 37 were chromophobe adenomata and 2 eosinophilic adenomata, and 1 showed clinical characteristics of both. There were 31 men and 9 women in the series. The average age at which the patient presented himself was forty-nine years. While the number of cases is small, the author believes the following conclusions are justified:

(1) Patients with pituitary adenoma, if the tumor is not too far advanced or cystic, show excellent responses to radiotherapy. If such cases are properly diagnosed and selected, one may expect as high as 90.2 per cent of the functional areas to exhibit improvement or maintenance of visual function. Improvement was noted in 62.2 per cent and maintenance in 28 per cent of the series reported. If one includes the "N" category (normal function to start with) together with the "O" category (maintenance of vision), the results are maintenance in 41.2 per cent, improvement in 50.8 per cent, and vision lost in 7.9 per cent.

Even 28.0 per cent of maintained vision must not be taken lightly, since the cases selected were not too severely affected to begin with, and, particularly

in an older person, such maintenance is indeed a satisfactory result. Its value becomes even greater when one considers the additional risks of surgery, however skilled the surgeon.

(2) A slow type of treatment guided by frequent visual examinations has been found quite satisfactory. The frequent check of the quality of the entire field leaves little danger of serious, undetected loss. In addition to serving as an index for dosage and frequency of treatment, such examination furnishes the neurosurgeon with an accurate gauge whereby surgery may always be undertaken in plenty of time to avoid serious loss of visual function.

(3) In some cases improvement may occur during treatment (10 out of 20 cases), but it may not take place until some months after therapy has been completed. While 44 per cent of improvement occurred during the first year after the beginning of treatment, 37 per cent occurred during the second year, and a considerable proportion of this 37 per cent was delayed as long as a year after treatment has been completed. Some improvement was demonstrated even during the third and fourth years after the beginning of treatment, corresponding to two and a half and three and a half years after its completion. When administering radiotherapy for pituitary adenoma, therefore, if no serious visual loss threatens the patient, one should allow at least four to six months to elapse after the completion of treatment before concluding that no improvement will take place, and at least two to three years before judging the total amount of improvement.

Nine figures; 3 tables.

Thyroid Neoplasms Following Irradiation. G. M. Wilson, R. Kilpatrick, H. Eckert, R. C. Curran, R. P. Jepson, G. W. Blomfield, and H. Miller. Brit. M. J. **2:** 929–934, Oct. 18, 1958. (University of Sheffield, Sheffield, England)

Nine cases of thyroid neoplasm are described in patients who had previously received irradiation to the neck. Seven of these patients had carcinoma, and in 2 the histologic diagnosis was premalignant thyroid adenoma.

Six of the carcinoma patients had been exposed in childhood (in the course of irradiation of cutaneous lesions) to a calculated thyroid dose varying from 130 to 2,700 r. The latent period in these cases was from five to eighteen years, and the carcinoma invariably developed in that part of the thyroid receiving the highest dose. The other carcinoma patient was irradiated for thyrotoxicosis at the age of twenty-six, and an anaplastic carcinoma of the thyroid developed thirty-seven years later.

In 1 patient a thyroid adenoma appeared fourteen years after treatment with radium needles for a nevus of the neck at the age of three. The thyroid dose was probably 1,000 r. The other adenoma patient received a probable thyroid dose of 2,000 r or more at the age of twenty-one for thyrotoxicosis. The adenoma was noted twenty years later.

The authors review the evidence regarding association of irradiation and subsequent development of carcinoma and conclude that exposure in childhood predisposes to the appearance of thyroid neoplasms. The association following exposure in adults is less certain.

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Carcinoma of the Thyroid Following Irradiation. A. W. G. Goolden. Brit. M. J. **2:** 954–955, Oct. 18, 1958. (Hammersmith Hospital, London, England)

The author reports 3 cases of carcinoma of the thyroid following irradiation of the neck.

The first patient had been treated for thyrotoxicosis at the age of eighteen and was seen with follicular thyroid carcinoma at the age of thirty-six.

In the second case tuberculous lymphadenitis had been treated by irradiation of the neck at the age of eleven. A follicular thyroid carcinoma was diagnosed thirty-eight years later. At that time there was a history of a thyroid mass for twelve years.

The third patient had been treated for exophthalmic goiter when twenty-eight years old. At sixty-nine years a follicular carcinoma was resected.

The author does not give the irradiation dose to the thyroid in any of these cases but notes that in 2 cases there was some damage to the skin and subcutaneous tissues of the neck. He concludes that these tumors were probably radiation-induced and points out that a large scale survey of thyroid carcinomas in previously irradiated necks is necessary to evaluate fully this relationship.

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Aplasia of a Breast after Deep Roentgen Therapy for a Mediastinal Sarcoma. Ch. M. Gros and R. Keiling. J. de radiol. **39:** 636–637, October 1958. (In French) (Strasbourg, France)

A ten-year-old girl was seen with a small-cell sarcoma on the right side of the mediastinum. Deep roentgen therapy was given after surgical extirpation.

At the age of thirteen it was quite obvious that normal breast tissue was developing on the left but that the right breast was very small. Roentgenograms were taken at the age of fifteen to compare the two sides. Apparently the roentgen therapy had stopped the growth of the active breast tissue. This is a rather unusual occurrence, and the authors were able to find only about 10 cases in previous medical literature.

Two roentgenograms; 2 photographs.

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Radiation Nephritis. A Clinicopathologic Correlation of Three Surviving Cases. Sheldon R. Cogan and Israel I. Ritter. Am. J. Med. **24:** 530–534, April 1958. (Michael Reese Hospital, Chicago 16, Ill.)

The authors report 3 nonfatal cases of radiation nephritis, with particular attention to the renal histology. Two patients were adults, and renal tissue was obtained by percutaneous biopsy. The third patient was a child, and nephrectomy was performed when a nonfunctioning left kidney and hypertension developed following massive irradiation.

These 3 cases are the only instances of radiation nephritis encountered at the Michael Reese Hospital (Chicago). So far as can be estimated, the patients did not receive a larger amount of radiation than was given to other patients receiving similar treatment. Just why nephritis developed is not known. Individual variation in susceptibility of the renal tissue to radiation and errors in dosage are mentioned as possibilities. It is suggested that the apparent rarity of the condition is due to a lack of awareness of its existence by the clinician and roentgenologist. It is

important to establish the true incidence so that steps may be taken to prevent its occurrence.

Three photomicrographs.

Acute Radiation Nephritis in Childhood. J. Swanson Beck. Brit. M. J. **2:** 489–490, Aug. 23, 1958. (Western Infirmary, Glasgow, Scotland)

A child of two and a half years had a Wilms tumor, which was removed surgically, after which a four-week course of radiotherapy (3,250 r) was given to the left renal area. Ten months later a metastasis in the perirenal fat on the right was discovered and radiotherapy was again given, 3,000 r to the right renal area in three weeks. In three months symptoms of acute nephritis appeared and death ensued.

The patient had a severe acute hemolytic anemia with well marked anisocytosis, polychromasia, poikilocytosis, and abundant "burr" cells in the peripheral blood. This blood picture, not previously described in acute radiation nephritis, is considered to be merely another manifestation of the fulminating uremia.

Postmortem findings are included.

Two photomicrographs.

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Hypertension Following X-Irradiation of the Kidneys. Clifford Wilson, J. M. Ledingham, and M. Cohen. Lancet **1:** 9–16, Jan. 4, 1958. (Radiotherapy Department, London Hospital, London E.1, England)

For many years it has been known that x-irradiation may damage the kidneys, but the clinical importance of this has been recognized only recently (see, for example, Hartman *et al.*: Am. J. M. Sc. **172:** 487, 1926, and Radiology **8:** 142, 1927; Kunkler *et al.*: Brit. J. Radiol. **25:** 190, 1952 Abst. in Radiology **60:** 326, 1953; Paterson: J. Fac. Radiologists **3:** 270, 1952. Abst. in Radiology **60:** 326, 1953; Luxton: Quart. J. Med. **22:** 215, 1953; Editorial by Carpender: Radiology **61:** 649, 1953; Bennett *et al.*: Radiology **61:** 411, 1953).

From their own observations in man and experimental studies in the rat, the authors conclude that irradiation of the kidneys has two distinct and independent biological effects: (1) interstitial fibrosis and (2) hypertension. Both in man and in the rat these effects may develop together or separately. When they are associated, the structural changes in the kidney present a composite picture of the results of interstitial fibrosis and of hypertensive vascular damage. The two effects have different time relations. Under the conditions which give rise to interstitial fibrosis this process is far advanced when the blood pressure first rises. Hypertension, on the other hand, takes four to nine months to develop in the rat, a latent interval similar to that observed in man.

In the rat, as in man, there are many parallels between this and other forms of renal hypertension. Thus, irradiation of one kidney produces hypertension, and removal of the irradiated kidney may bring the blood pressure back to normal. Secondary hypertensive lesions appear in the opposite kidney, and there seems to be a relation between severity of hypertension and extent of these secondary lesions.

The most important conclusion from the authors' observations is that, in both man and rat, hypertension may be produced by irradiation of the kidney in the absence of structural changes usually found in irradiation sclerosis. Later, structural changes do occur, but both in man and in the rat they closely resemble the lesions of essential malignant hypertension, and they must be regarded as secondary to the high blood pressure. The experiments provide evidence, therefore, that renal hypertension can develop without any preceding anatomical lesion, at any rate as revealed by direct microscopy. Certainly there are none of the anatomical changes in the kidney which are known to produce high blood pressure in man or in laboratory animals.

The present experiments do not indicate how renal irradiation produces hypertension, nor is it known what factors determine the development of irradiation sclerosis on one hand or hypertension on the other, or indeed the two effects together.

The authors report two cases, illustrating the two distinct patterns of renal structural damage.

Twelve figures; 1 table.

An editorial in the same issue of Lancet (**1:** 33, Jan. 4, 1958) entitled "Incidental Dangers of X-ray Therapy" emphasizes the need for close co-operation between the radiotherapist and clinician, surgeon, or gynecologist. "Radiotherapy remains a powerful weapon which can be fatal to both friend and foe; and the whole resources of medicine are required to ensure that its edge is turned always against the invader."

Irradiation Cystitis. Thomas L. Pool. J.A.M.A. **168:** 854–856, Oct. 18, 1958 (Mayo Clinic, Rochester, Minn.)

Fifty cases of irradiation cystitis were seen between 1950 and 1954 at the Mayo Clinic. It is not known whether any specific form of irradiation is responsible for this complication. No correlation has been noted between the amount of therapy and the intensity of the reaction. Individual sensitivity appears to vary greatly. No decade of life seems to be immune and there is no preponderance of reactions in any one decade. Of the 50 patients, 22 showed a reaction within the first year after irradiation, 8 in the second year, 5 in the third, 4 in the fourth, 2 in the fifth, 3 in the sixth, and 1 in the eighth. In 3 cases the reaction was delayed until the eleventh, twelfth, and fourteenth year, respectively.

There seems to be no doubt that the cause is impaired circulation to the involved area of the bladder, with superimposed infection. Later there may be ulceration followed by fistula formation or scarring.

When radium has been used, the most common site is the posterior wall in the midline and just back of the intraureteric ridge. When a vesicovaginal fistula is present, this ridge is the usual site of opening into the bladder.

Thirty of the author's patients had gross hematuria as the predominant urinary symptom. Others had dysuria, frequency, and urgency.

Treatment is essentially symptomatic and consists of antibacterial agents for the superimposed infection and argyrol gavage. Urinary diversion procedures even in the face of fistula are discouraged.

Thirty-one of the patients did not require any treatment. In 18 of these no further symptoms developed. The others had recurrences. Nineteen required treatment and 12 of these remain symptom-free.

MAJ. MARTIN A. THOMAS, M.C.
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Factors Influencing the Incidence of Leukemia: Special Consideration of the Role of Ionizing Radiation. E. E. Schwartz and A. C. Upton. Blood **13:** 845-864, September 1958. (Oak Ridge National Laboratory, Oak Ridge, Tenn.)

The recorded incidence of leukemia and lymphomas has become markedly higher during the past thirty years. During the same interval the amount of ionizing radiation in the environment has been steadily increased by man-made additions to the natural background. The possibility that radiation may account in part for the rising incidence of leukemia is suggested by the more frequent development of the disease in those exposed to large amounts of radiation.

Although the extent of increase in the risk of leukemia cannot be determined accurately from the recorded rates and the relation between leukemia incidence and radiation dose cannot be estimated precisely, it appears probable that radiation is only one of the many environmental agents influencing the occurrence of the disease. Other factors associated with the changing standard of living, such as the increasing use of marrow-depressing drugs and the growing contamination of the atmosphere with chemical pollutants, deserve further investigation as leukemogenic influences.

Four figures; 8 tables.

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Thorotrast Disease. Jayme Landman and Nicola C. Caminha. Bol. da Soc. brasil. de radiol. **2:** 99-104, March-April 1958. (In Portuguese) (Clínica Médica da Fac. de Ciências Médicas, Rio de Janeiro, Brasil)

The retention of Thorotrast causes opacification of the spleen, visible on roentgenograms. This must be differentiated from calcifications due to other causes, such as infectious and parasitic diseases (malaria, tuberculosis, schistosomiasis, leishmaniasis), blood dyscrasias in which phleboliths from splenic infarcts occur (hemolytic icterus, severe anemia, polycythemia vera), tumors (hemangioma), pseudo-tumors (echinococcosis or other calcified cysts), etc.

A solution of 25 per cent thorium dioxide was first used in 1929 as a roentgenographic contrast medium by Oka (Japan) and Radt (Germany); it was popularized for cerebral angiography by Egas Moniz in 1931. Since 1932 it has been known that colloidal thorium dioxide, when injected into animals, is stored permanently in the liver, with resultant granuloma and focal necrobiosis, as well as in the bone marrow, adrenals, lymph nodes, spleen, lungs—in fact, within the entire reticuloendothelial system. Thorotrast has an emission of alpha particles and, even though actual radiation levels are difficult to evaluate, the average dose of contrast material has been estimated to correspond to 14 r (total body load?) daily, shortly after the injection, being reduced to about 3 r daily within one year. If the entire dose were to remain in a circumscribed area, the figure might be as high as 30 r daily.

Frühling has classified the possible harmful consequences of Thorotrast injection as (*a*) formation of "thorastoma" either at the site of injection or along the trajectory of penetration; (*b*) generalized "thorastosis," due to retention in and involvement of various organs (as hepatosplenic cirrhosis), (*c*) association of "thorastoma" and "thorastosis," and (*d*) association of either or both "thorastoma" and "thorastosis" with a specific tumor (epithelioma of the bronchus, common biliary duct, or kidney pelvis; sarcoma of liver, spleen, or soft tissues at the site of injection).

The diagnosis of Thorotrast disease is based on the history, observation of typical opacification of liver and spleen, abdominal roentgenography, autoradiography, use of the Geiger counter, and autopsy and biopsy reports.

In one of the 2 specific cases reported in this paper, use of a scintillation counter revealed that, when the background was taken as a base line (100), there were 15.3 per cent more counts over the spleen, 11.3 per cent more counts over the right hip, and 11.3 per cent more counts over the left lobe of the liver. No evidence of actual Thorotrast disease had as yet appeared in either of these 2 patients, both of whom gave a history of injection (*i.e.*, retention) of thorium dioxide and showed characteristic splenic opacification on abdominal roentgenograms.

Two roentgenograms; 1 table.

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Acute Clinical Effects of Penetrating Nuclear Radiation. Herbert B. Gerstner. J.A.M.A. **168:** 381-388, Sept. 27, 1958. (Route 3, Box 512 C, San Antonio, Texas)

Four sources of information—atomic bomb casualties, nuclear accidents, radiotherapy, and animal experiments—were used in this study of the effects of penetrating nuclear radiation.

The prodromal phase, reaching its height about eight hours after exposure, is not necessarily indicative of the seriousness of the ensuing specific organ responses. It is easily influenced by individual disposition and psychological factors. It resembles motion sickness with anorexia, listlessness and apathy, leading to nausea and vomiting. This phase is transient, usually subsiding in the first twenty-four hours and at the most in forty-eight hours.

The specific organ responses—central nervous system, gastrointestinal, and hematopoietic—are described and discussed. The threshold dose, the latent period, the characteristic signs and symptoms, the underlying pathology, the time of death (if occurring), the cause of death, and prognosis, are considered. In general, the prognosis of the cerebral form is hopeless and that of the gastrointestinal form poor. The basic rules for medical defense planning will probably be dictated by the hematopoietic form.

Six charts; 3 tables.

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A Simple Protection Device for Urologic Units. Joseph E. Whitley. J. Urol. **80:** 277-278, October 1958. (Bowman Gray School of Medicine, Winston-Salem, N. C.)

In addition to the usual protective devices used during retrograde urography, such as the lead apron (0.3 mm. Pb equivalent), 3 mm. added Al filtration, and Pb shields over the testes of the patient, the author advocates a rectangular cone to avoid the unnecessarily large field required by a round cone. His cone measures 1 3/16 by 1 7/16 in. at the base; it is 6 in. long and measures 3 1/2 by 4 1/4 in. at the distal end. The body of the cone is made of 3/16-in. steel and the base plate is of 1/4 in. steel.

Prior to the installation of this cone, casual measurements gave readings of up to 200 milliroentgens per exposure to the wrist of the surgeon, with an average of 22 mr. The anterior thorax received up to 27 mr. per exposure with an average of 7 mr. Following the installation of the rectangular cone no measured exposure was obtained on the wrist and anterior thorax. The quality of the radiographs obtained with the new cone was also improved.

One photograph; 3 diagrams.

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EXPERIMENTAL STUDIES

Supportive Therapy to Animals Exposed to Whole Body Irradiation. Creighton A. Hardin, Alvar A. Werder, Tom H. McGuire, and Donald R. Woodson. Surg., Gynec. & Obst. **107:** 508–510, October 1958. (University of Kansas Medical Center, Kansas City, Kans.)

The authors report a series of experiments devised to study the comparative effects of serum, whole blood, and saline as supportive agents in irradiated mice. Single whole-body doses of 500, 600, 650, and 700 r were delivered to CFW mice weighing an average of 20 gm. All experiments were repeated at thirty days.

The only survivors of the control series were 6 of 41 mice receiving 500 r. Human whole blood, human serum, heated human serum, and saline were injected intraperitoneally in different doses and at different intervals. Survival was enchanced by all of these agents.

The authors conclude that the injection of blood, serum, and saline all contribute to survival of mice through a supportive systemic effect and that all were equally effective.

Seven tables.

DAVID J. RITCHIE, M.D.
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Studies with Transplantable AK4 Mouse Leukemia. III. Effect of Spleen and Marrow Shielding on AK4 Leukemic Implants in Homologous Strains of Irradiated Mice. Irene U. Boone, Betty S. Rogers, and Payne S. Harris. J. Nat. Cancer Inst. **21:** 513–522, September 1958. (Los Alamos Scientific Laboratory, Los Alamos, N. Mex.)

Continuing earlier studies on AK4 leukemia (Radiation Res. **5:** 450; 459, October 1956. Abst. in Radiology **69:** 319, 1957) the authors investigated the effects of spleen and marrow shielding on implants in homologous strains of irradiated mice. A/*St* and C57BL female mice between eight and sixteen weeks of age were used. These strains were chosen (1) because it has been possible to demonstrate in them a linear relationship between the log dose of radiation and the probit of per cent leukemia "takes" (in this case, equivalent to mortality) eleven days after injection of AK4 leukemia and (2) because the spleen of the C57BL mouse has little hematopoietic activity compared to other strains and morphological differences between the strains may indicate the tissue or cell that is most involved or responsible in protective mechanisms. The AK4 leukemia was obtained from the Sloan-Kettering Institute and maintained in the AKR strain of mice by weekly transplants.

Anesthesia was used in the spleen-shielded studies but not in those animals in which the femoral bone marrow was protected. Radiation doses ranged from 100 to 800 rads and the following groups of 20 mice each were included in each shielding study: (1) irradiated with shielding and inoculated with AK4 leukemia; (2) irradiated without shielding and inoculated with AK4 leukemia; (3) irradiated with shielding and inoculated with normal AKR spleen homogenate; (4) irradiated without shielding and inoculated with normal AKR spleen homogenate; (5) unirradiated and inoculated with AK4 leukemia; (6) unirradiated and inoculated with normal AKR spleen homogenate. The spleen homogenate inoculation (leukemic or normal) was administered twenty-four hours after irradiation. The radiation dose required to produce a 50 per cent incidence of deaths due to leukemia was calculated on the basis of leukemic deaths at twelve days postirradiation.

The results of the experiments with irradiated animals that did not receive leukemia indicated that, although a protective effect was produced by either spleen or femur shielding in both strains, there were no significant quantitative differences afforded by the tissue shielded in either strain. Resistance to transplantable leukemia was partially protected by femur shielding in the irradiated mice of both strains and by spleen shielding in the irradiated A/*St* mice. However, in the irradiated C57BL animals that received leukemia, there was no significant difference between the spleen-shielded and nonshielded groups. The difference in the spleen-shielding results between the A/*St* and C57BL mice tends to indicate that greater protection was associated with myelopoietic tissue than with lymphoid tissue.

Eight figures; 1 table.

A Comparison of the Effects on the Shwartzman Phenomenon of Leukopenia Produced by Nitrogen Mustard and by Whole Body Irradiation. Douglas E. Johnstone and Joe W. Howland. J. Exper. Med. **108:** 431–440, Oct. 1, 1958. (University of Rochester School of Medicine and Dentistry, Rochester, N. Y.)

The effect of leukopenia on the susceptibility to the localized Shwartzman reaction was studied in rabbits receiving whole-body irradiation and nitrogen mustard respectively. In only 17 per cent of animals receiving nitrogen mustard in which the total polymorphonuclear leukocyte count was less than 100 cells/c.mm. were positive local Shwartzman reactions observed, whereas 75 per cent of irradiated animals having total polymorphonuclear leukocyte counts less than 100 cells/c.mm. had positive reactions. A local Shwartzman reaction occurred in 60 of 71 control rabbits (85 per cent). Animals of both the treated groups showed positive Shwartzman reactions at a time when their total polymorphonuclear leukocyte counts were less than 500 cells/c.mm.

From the findings, it is concluded (*a*) that the presence of normal numbers of circulating polymorphonuclear leukocytes is not an obligatory prerequisite to the localized hemorrhagic necrosis of the Shwartzman phenomenon, and (*b*) that the mechanism of action of nitrogen mustard and whole-body irradiation on body tissues differ in relation to the Shwartzman reaction.

Six photomicrographs; 2 graphs; 2 tables.